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Patentanmeldung Nr. Patent application No. Demande de brevet n°

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Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
p.o.

R C van Dijk

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(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.
If no title is shown please refer to the description.
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Methods and nucleic acids for the analysis od CpG dinucleotide methylation status associated with the development of prostate cancer

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METHODS AND NUCLEIC ACIDS FOR THE ANALYSIS OF CpG DINUCLEOTIDE METHYLATION STATUS ASSOCIATED WITH THE DEVELOPMENT OF PROSTATE CANCER

FIELD OF THE INVENTION

The present invention relates to human DNA sequences that exhibit altered methylation patterns (hypermethylation or hypomethylation) in prostate cancer patients. Particular embodiments of the invention provide highly accurate methods for detection and differentiation of prostate carcinomas.

BACKGROUND

Correlation of aberrant DNA methylation with cancer. Aberrant DNA methylation within CpG 'islands' is characterized by *hyper-* or *hypomethylation* of CpG dinucleotide sequences leading to abrogation or over expression of a broad spectrum of genes, and is among the earliest and most common alterations found in, and correlated with human malignancies. Additionally, abnormal methylation has been shown to occur in CpG-rich regulatory elements in both intronic and coding parts of genes for certain tumors. In colon cancer, aberrant DNA methylation constitutes one of the most prominent alterations and inactivates many tumor suppressor genes including, *inter alia*, p14ARF, p16INK4a, THBS1, MINT2, and MINT31 and DNA mismatch repair genes such as hMLH1.

Aside from the specific hypermethylation of tumor suppressor genes, an overall hypomethylation of DNA can be observed in tumor cells. This decrease in global methylation can be detected early, far before the development of frank tumor formation. A correlation between hypomethylation and increased gene expression has been determined for many oncogenes.

Prostate cancer. Prostate cancer is the most common malignancy among men in the United States (~200,000 new cases per year), and the sixth leading cause of male cancer-related

deaths worldwide (~204,000 per year) . Prostate cancer is primarily a disease of the elderly, with approximately 16% of men between the ages of 60 and 79 having the disease. According to some estimates at autopsy, 80% of all men over 80 years of age have some form of prostate disease (eg cancer, BPH, prostatitis, etc). Benign prostate hypertrophy is present in about 50% of men aged 50 or above, and in 95% of men aged 75 or above. It is obvious from these reports that prostate cancer is often not a disease that men die from, but with. Recent evidence suggests that the incidence of prostate cancer may in fact be declining, likely as result of better treatment, better surgery, and earlier detection.

Diagnosis and prognosis of prostate cancer; deficiencies of prior art approaches. Current guidelines for prostate cancer screening have been suggested by the American Cancer Society and are as follows: At 50 years of age, health care professionals should offer a blood test for prostate specific antigen (PSA) and perform a digital rectal exam (DRE). It is recommended that high risk populations, such as African Americans and those with a family history of prostate disease, should begin screening at 45 years of age. Men without abnormal prostate pathology generally have a PSA level in blood below 4ng/ml. PSA levels between 4ng/ml and 10ng/ml (called the „Grey Zone") have a 25% chance of having prostate cancer. The result is that 75% of the time, men with an abnormal DRE and a PSA in this grey zone have a negative, or a seemingly unnecessary biopsy. Above the grey zone, the likelihood of having prostate cancer is significant (> 67%) and increases even further as PSA levels go up. Numerous methods exist for measuring PSA (percent-free PSA, PSA velocity, PSA density, etc..), and each has an associated accuracy for detecting the presence of cancer. Yet, even with the minor improvements in detection, and the reported drops in mortality associated with screening, the frequency of false positives remains high. Reduced specificity results in part from increased blood PSA associated with BPH, and prostatis. It has also been estimated that up to 45% of prostate biopsies under currrent guidelines are falsely negative, resulting in decreased sensitivity even with biopsy.

TRUS guided biopsy is considered the gold standard for diagnosing prostate cancer. Recommendations for biopsy are based upon abnormal PSA levels and or an abnormal DREs. For PSA there is a grey zone where a high percentage of biopsies are perhaps not necessary. Yet the ability to detect cancer in this grey zone (PSA levels of 4.0 to 10 ng/ml) is difficult without biopsy. Due to this lack of specificity, 75% of men undergoing a biopsy do not have cancer (25). Yet without biopsy, those with cancer would be missed, resulting in increased morbidity and mortality. However the risks associated with an unecessary biopsy are also high.

It is clear that there is a need for an early, specific prostate cancer test for more accurate detection and treatment monitoring, to improve morbidity and mortality rates.However, using routine histological examination, it is often difficult to distinguish benign hyperplasia of the prostate from early stages of prostate carcinoma, even if an adequate biopsy is obtained (McNeal J. E. et al., *Hum. Pathol.* 2001, 32:441-6). Furthermore, small or otherwise insufficient biopsy samples often impede the analysis.

Molecular markers would offer the advantage that they could be used to efficiently analyze even very small tissue samples, and samples whose tissue architecture has not been maintained. Within the last decade, numerous genes have been studied with respect to differential expression among benign hyperplasia of the prostate and different grades of prostate cancer. However, no single marker has as yet been shown to be sufficient for the diagnosis of prostate tumors in a clinical setting.

Alternatively, high-dimensional mRNA-based approaches may, in particular instances, provide a means to distinguish between different tumor types and benign and malignant lesions. However, application of such approaches as a routine diagnostic tool in a clinical environment is impeded and substantially limited by the extreme instability of mRNA, the rapidly occurring expression changes following certain triggers (*e.g.*, sample collection), and, most importantly, by the large amount of mRNA needed for analysis which often cannot be obtained from a routine biopsy (see, *e.g.*, Lipshutz, R. J. et al., *Nature Genetics* 21:20-24, 1999; Bowtell, D. D. L. *Nature Genetics Suppl.* 21:25-32, 1999).

The GSTP1 gene. The core promoter region of the Gluthione S-Transferase P gene (GSTP1; accession no. NM_000852) has been shown to be hypermethylated in prostate tumor tissue. The glutathione S-transferase pi enzyme is involved in the detoxification of electrophilic carcinogens, and impaired or decreased levels of enzymatic activity (GSTP1 impairment) have been associated with the development of neoplasms, particularly in the prostate. Mechanisms of GSTP1 impairment include mutation (the GSTP*B allele has been associated with a higher risk of cancer) and methylation.

Prior art GSTP1 studies. Lee et al., in United States Patent No 5,552,277, disclosed that the expression of the gluthione-S-transferase (GST) Pi gene was downregulated in a significant proportion of prostate carcinomas. Moreover, by means of restriction enzyme analysis they were able to show that the promoter region of the of the GSTP1gene was upmethylated (hypermethylated) in prostate carcinomas as opposed to normal prostate and leukocyte tissue. However, due to the limited and imprecise nature of the analysis technique

used (HpaII digestion, followed by Southern blotting) the exact number and position of the methylated CG dinucleotides were not characterized.

Douglas et al. (WO9955905) used a method comprising bisulfite treatment, followed by methylation specific PCR to show that prostate carcinoma-specific GSTP1 hypermethylation was localized to the core promoter regions, and localized a number of CpG positions that had not been characterised by Lee et al.

Herman and Baylin (United States Patent No. 6,017,704) describe the use of methylation specific primers for methylation analysis, and describe a particular primer pair suitable for the analysis of the corresponding methylated GSTP1promoter sequence.

However, with respect to the use of GSTP1markers, the prior art is limited with respect to the number of GSTP1 promoter CpG sequences that have been characterized for differential methylation status. Moreover, there are no disclosures, suggestions or teachings in the prior art of how such markers could be used to distinguish among benign hyperplasia of the prostate and different grades of prostate cancer. Furthermore, GSTP1 has been shown to be methylated in other cancers. For this reason it is critical to identify markers other than GSTP1 that have high performance values in the prostate, but not other organs.

Aberrant genetic methylation in prostate cancer has also been observed in several other genes including AR, p16 (CDKN2a/INK4a), CD44, CDH1. Genome wide hypomethylation for example of the LINE-1 repetitive element has also been associated with tumor progression (Santourlidis S ,Florl A ,Ackermann R ,Wirtz HC ,Schulz WA 'High frequency of alterations in DNA methylation in adenocarcinoma of the prostate.' Prostate 1999 May 15; 39(3): 166-74).

However, use of these genes as alternative or supplemental diagnostic, or otherwise clinically useful markers in a commercial setting has not been enabled. The application of differentially methylated genes to clinically utilizable platforms requires much further investigation into the sensitivity and specificity of the genes. For example, in the case of the gene CD44, a known metastasis suppressor, downregulation was associated with hypermethylation. However the use of this gene as a commercially available marker was not enabled as it was also methylated in normal tissues. See Vis AN Oomen M Schroder FH van der Kwast TH 'Feasibility of assessment of promoter methylation of the CD44 gene in serum of prostate cancer patients.' Mol Urol. 2001 Winter;5(4):199-203.

Pronounced need in the art. Therefore, in view of the incidence of prostate hyperplasia (50% of men aged 50 or above, and 95% of men aged 75 or above) and prostate cancer (180 per 100,000), there is a substantial need in the art for the development of

molecular markers that could be used to effectively detect prostate cell proliferative disorders, in particular prostate carcinoma. There is also a particular need in the art for a means of distinguishing benign hyperplasia of the prostate and prostate cancer. Additionally, there is a pronounced need in the art for the development of molecular markers that could be used to provide sensitive, accurate and non-invasive methods (as opposed to, e.g., biopsy and transrectal ultrasound) for the diagnosis of and differentiation between prostate cell proliferative disorders.

SUMMARY OF THE INVENTION

The present invention provides a method for ascertaining genetic and/or epigenetic parameters of genomic DNA. The method has utility for the improved diagnosis, treatment and monitoring of prostate cell proliferative disorders, more specifically by enabling the improved identification of and differentiation between subclasses of said disorder and the genetic predisposition to said disorders. The present invention provides novel methods for detecting and/or distinguishing between prostate cell proliferative disorders. The invention provides methods for the analysis of biological samples for features associated with the development of prostate cell proliferative disorders, in particular benign prostate hyperplasia (hereinafter also referred to as BPH) and prostate carcinoma, the method thereby enables the early detection of prostate carcinomas and their differentiation from benign cell proliferative disorders of the prostate, including BPH. The method is characterised in that at least one nucleic acid, or a fragment thereof, from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 295 is/are contacted with a reagent or series of reagents capable of distinguishing between methylated and non methylated CpG dinucleotides within the genomic sequence, or sequences of interest.

In a particularly preferred embodiment said method enables the differentiation between non-cancerous types of prostate tissue (including BPH and normal) and prostate carcinoma. In a further embodiment the method enables the differentiation of prostate cancer from normal prostate tissue, tissues originating from other tissues and BPH. In a further embodiment the method enables the differentiation of prostate cancer form cancers originating from other tissues. The invention presents improvements over the state of the art in that it enables a highly specific classification of prostate cell proliferative disorders, thereby allowing for improved and informed treatment of patients. In particular it allows for the differentiation of BPH from prostate carcinoma. The invention provides further improvements

over the state of the art in that said method may be used for the analysis of bodily fluids including post prostatic massage urine, ejaculate, urine, or blood, it therefore enables a non invasive means for the detection and/or differentiation of prostate cell proliferative disorders.

Preferably, the source of the test sample is selected from the group consisting of cells or cell lines, histological slides, biopsies, paraffin-embedded tissue, bodily fluids, ejaculate, urine, blood, and combinations thereof. More preferably, the source is bodily fluids, post prostatic massage urine, ejaculate, urine, or blood.

Specifically, the present invention provides a method for detecting prostate cell proliferative disorders, comprising: obtaining a biological sample comprising genomic nucleic acid(s); contacting the nucleic acid(s), or a fragment thereof, with one reagent or a plurality of reagents sufficient for distinguishing between methylated and non-methylated CpG dinucleotide sequences within at least one target sequence of the subject nucleic acid, wherein the target sequence comprises, or hybridizes under stringent conditions to, a sequence comprising at least 16 contiguous nucleotides of at least one sequence taken from the group consisting SEQ ID NO: 1 to 295, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence; and determining, based at least in part on said distinguishing, the methylation state of at least one target CpG dinucleotide sequence, or an average, or a value reflecting an average methylation state of a plurality of target CpG dinucleotide sequences. Preferably, distinguishing between methylated and non methylated CpG dinucleotide sequences within the target sequence comprises methylation state-dependent conversion or non-conversion of at least one such CpG dinucleotide sequence to the corresponding converted or non-converted dinucleotide sequence within a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and contiguous regions thereof corresponding to the target sequence.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that the target sequence(s) comprise, or hybridizes under stringent conditions to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that the target sequence(s) comprise, or hybridizes under stringent conditions to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences

according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that the target sequence(s) comprise, or hybridizes under stringent conditions to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Additional embodiments provide a method for the detection of prostate cell proliferative disorders, comprising: obtaining a biological sample having subject genomic DNA; extracting the genomic DNA; treating the genomic DNA, or a fragment thereof, with one or more reagents to convert 5-position unmethylated cytosine bases to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties; contacting the treated genomic DNA, or the treated fragment thereof, with an amplification enzyme and at least two primers comprising, in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof, wherein the treated DNA or the fragment thereof is either amplified to produce an amplificate, or is not amplified; and determining, based on a presence or absence of, or on a property of said amplificate, the methylation state of at least one CpG dinucleotide sequence selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 59 , or an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotide sequences thereof.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that the target sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that the target sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that the target sequence(s) comprise, or hybridizes to, one or

more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Preferably, at least one such hybridizing nucleic acid molecule or peptide nucleic acid molecule is bound to a solid phase. Preferably, determining comprises use of at least two methods selected from the group consisting of: hybridizing at least one nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof; hybridizing at least one nucleic acid molecule, bound to a solid phase, comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof; hybridizing at least one nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof, and extending at least one such hybridized nucleic acid molecule by at least one nucleotide base; and sequencing of the amplificate.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that said nucleotide sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that said nucleotide sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that said nucleotide sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

For all said embodiments the following embodiments are particularly preferred. Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that the target sequence(s) comprise, or hybridizes under stringent conditions to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that the target sequence(s) comprise, or hybridizes under stringent conditions to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Further embodiments provide a method for the analysis of prostate cell proliferative disorders, comprising: obtaining a biological sample having subject genomic DNA; extracting the genomic DNA; contacting the genomic DNA, or a fragment thereof, comprising one or more sequences selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 59 or a sequence that hybridizes under stringent conditions thereto, with one or more methylation-sensitive restriction enzymes, wherein the genomic DNA is either digested thereby to produce digestion fragments, or is not digested thereby; and determining, based on a presence or absence of, or on property of at least one such fragment, the methylation state of at least one CpG dinucleotide sequence of one or more sequences selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 59 , or an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotide sequences thereof. Preferably, the digested or undigested genomic DNA is amplified prior to said determining.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that said nucleotide sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that said nucleotide sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table

5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that said nucleotide sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Additional aspects of the invention provide novel genomic and modified nucleic acid sequences, as well as oligonucleotides and/or PNA-oligomers for analysis of cytosine methylation patterns within sequences from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 59 .

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1 to 3 are ranked matrices produced from bisulfite sequencing data. The overall matrix represents the sequencing data for one fragment. Each row of the matrix represents a single CpG site within the fragment and each column represents an individual sample. The bar on the left represents a scale of the percent of methylation, with the degree of methylation represented by the shade of each position within the column from black representing 100% methylation to light grey representing 0% methylation. No data was available for white positions.

Figure 1 shows the sequencing data of a fragment of the gene Prostaglandin E2 Receptor, EP4 Subtype wherein the sequenced samples are from prostate carcinoma.

Figure 2 shows the sequencing data of a fragment of the gene Orphan Nuclear Receptor (a-1Fetoprotein Transcription Factor wherein the sequenced samples are from prostate carcinoma.

Figure 3 shows the sequencing data of a fragment of the gene 1-Acyl-SN-Glycerol-3-Phosphate Acyltransferase Gamma wherein the sequenced samples are from prostate carcinoma.

Figure 4 shows Normal prostate and BPH vs. Prostate Cancer marker rankings according to Example 3. Each individual genomic region of interest is represented as a point.The left plot gives uncorrected p-values from the genewise logistic regression model. Lower and upper dotted lines show 5% Bonferroni and FDR limits respectively. The X-axis shows the p values for the individual CpG positions. The p values are the probabilities that the observed distribution occurred by chance in the data set.

The right plot gives accuracy, sensitivity and specificity of a linear SVM trained on methylation measurements from all oligonucleotides. The accuracy of each genomic region is represented as black squares, the specificity as unfilled diamonds, the sensitivity as unfilled squares. The accuracy as measured on the X-axis shows the fraction of correctly classified samples.

Figure 5 shows the best 12 markers for Normal prostate and BPH vs. Prostate Cancer differentiation according to Example 3. Normal prostate and BPH samples are shown on the left. Prostate cancer is on the right. Each column represents one sample; each row one oligonucleotide. Oligonucleotides are grouped by candidate marker. The indicated markers are ordered from top to bottom with increasing accuracy. On the right side of each marker, Bonferroni corrected p-values are listed. Methylation data are centered and normalized to one standard deviation for individual oligonucleotides. The color represents the relative distance of the oligonucleotide methylation status from the mean value. Green color represents hypomethylated CpGs within an oligonucleotide while red indicates hypermethylated CpGs within an oligonucleotide.

Figure 6 shows Normal Prostate, BPH and Other Tissues vs. Prostate Cancer marker rankings according to Example 3. Each individual genomic region of interest is represented as a point.The left plot gives uncorrected p-values from the genewise logistic regression model. Lower and upper dotted lines show 5% Bonferroni and FDR limits respectively. The X-axis shows the p values for the individual CpG positions. The p values are the probabilities that the observed distribution occurred by chance in the data set. The right plot shows accuracy, sensitivity and specificity of a linear SVM trained on methylation measurements from all oligonucleotides. The accuracy of each genomic region is represented as black squares, the specificity as unfilled diamonds, the sensitivity as unfilled squares. The accuracy as measured on the X-axis shows the fraction of correctly classified samples.

Figure 7 shows the best 12 markers for Normal Prostate, BPH and Other Tissues vs. Prostate Cancer differentiation according to Example 3. Normal Prostate, BPH and Other Tissues samples are shown on the left. The 'Other Tissues' included normal tissue from other organs and cancer of other origins than prostate, according to table 7. Prostate cancer is on the right. Each column represents one sample; each row one oligonucleotide. Oligonucleotides are grouped by candidate marker. The indicated markers are ordered from top to bottom with increasing accuracy. On the right side of each marker, Bonferroni corrected p-values are listed. Methylation data are centered and normalized to one standard deviation for individual oligonucleotides. The color represents the relative distance of the oligonucleotide methylation

status from the mean value. Green color represents hypomethylated CpGs within an oligonucleotide while red indicates hypermethylated CpGs within an oligonucleotide.

Figure 8 shows Normal Prostate, BPH and Other Tissues vs. Prostate Cancer marker rankings according to Example 3. Each individual genomic region of interest is represented as a point.The left plot gives uncorrected p-values from the genewise logistic regression model. Lower and upper dotted lines show 5% Bonferroni and FDR limits respectively. The X-axis shows the p values for the individual CpG positions. The p values are the probabilities that the observed distribution occurred by chance in the data set. The following cancers are shown from left to right:bladder, melanoma, testes, kidney, endometrial cancer, lung, breast, pancreatic, liver, ovarian, salivary gland, and prostate.

DETAILED DESCRIPTION OF THE INVENTION

Definitions:

The term "CpG island" refers to a contiguous region of genomic DNA that satisfies the criteria of (1) having a frequency of CpG dinucleotides corresponding to an "Observed/Expected Ratio" >0.6, and (2) having a "GC Content" >0.5. CpG islands are typically, but not always, between about 0.2 to about 1 kb in length.

The term "methylation state" or "methylation status" refers to the presence or absence of 5-methylcytosine ("5-mCyt") at one or a plurality of CpG dinucleotides within a DNA sequence. Methylation states at one or more particular palindromic CpG methylation sites (each having two CpG CpG dinucleotide sequences) within a DNA sequence include "unmethylated," "fully-methylated" and "hemi-methylated."

The term "hypermethylation" refers to the average methylation state corresponding to an *increased* presence of 5-mCyt at one or a plurality of CpG dinucleotides within a DNA sequence of a test DNA sample, relative to the amount of 5-mCyt found at corresponding CpG dinucleotides within a normal control DNA sample.

The term "hypomethylation" refers to the average methylation state corresponding to a *decreased* presence of 5-mCyt at one or a plurality of CpG dinucleotides within a DNA sequence of a test DNA sample, relative to the amount of 5-mCyt found at corresponding CpG dinucleotides within a normal control DNA sample.

The term "microarray" refers broadly to both "DNA microarrays," and 'DNA chip(s),' as recognized in the art, encompasses all art-recognized solid supports, and encompasses all methods for affixing nucleic acid molecules thereto or synthesis of nucleic acids thereon. "Genetic parameters" are mutations and polymorphisms of genes and sequences further required for their regulation. To be designated as mutations are, in particular, insertions, deletions, point mutations, inversions and polymorphisms and, particularly preferred, SNPs (single nucleotide polymorphisms).

"Epigenetic parameters" are, in particular, cytosine methylations. Further epigenetic parameters include, for example, the acetylation of histones which, however, cannot be directly analyzed using the described method but which, in turn, correlate with the DNA methylation.

The term "bisulfite reagent" refers to a reagent comprising bisulfite, disulfite, hydrogen sulfite or combinations thereof, useful as disclosed herein to distinguish between methylated and unmethylated CpG dinucleotide sequences.

The term "Methylation assay" refers to any assay for determining the methylation state of one or more CpG dinucleotide sequences within a sequence of DNA.

The term "MS.AP-PCR" (Methylation-Sensitive Arbitrarily-Primed Polymerase Chain Reaction) refers to the art-recognized technology that allows for a global scan of the genome using CG-rich primers to focus on the regions most likely to contain CpG dinucleotides, and described by Gonzalgo et al., *Cancer Research* 57:594-599, 1997.

The term "MethyLight™" refers to the art-recognized fluorescence-based real-time PCR technique described by Eads et al., *Cancer Res.* 59:2302-2306, 1999.

The term "HeavyMethyl™" assay, in the embodiment thereof implemented herein, refers to a HeavyMethyl™ refer to the use of methylation specific *blocking* probes covering CpG positions between the amplification primers.

The term "Ms-SNuPE" (Methylation-sensitive Single Nucleotide Primer Extension) refers to the art-recognized assay described by Gonzalgo & Jones, *Nucleic Acids Res.* 25:2529-2531, 1997.

The term "MSP" (Methylation-specific PCR) refers to the art-recognized methylation assay described by Herman et al. *Proc. Natl. Acad. Sci. USA* 93:9821-9826, 1996, and by US Patent No. 5,786,146.

The term "COBRA" (Combined Bisulfite Restriction Analysis) refers to the art-recognized methylation assay described by Xiong & Laird, *Nucleic Acids Res.* 25:2532-2534, 1997.

The term "MCA" (Methylated CpG Island Amplification) refers to the methylation assay described by Toyota et al., *Cancer Res.* 59:2307-12, 1999, and in WO 00/26401A1.

The term "hybridization" is to be understood as a bond of an oligonucleotide to a complementary sequence along the lines of the Watson-Crick base pairings in the sample DNA, forming a duplex structure.

"Stringent hybridization conditions," as defined herein, involve hybridizing at 68°C in 5x SSC/5x Denhardt's solution/1.0% SDS, and washing in 0.2x SSC/0.1% SDS at room temperature, or involve the art-recognized equivalent thereof (e.g., conditions in which a hybridization is carried out at 60°C in 2.5 x SSC buffer, followed by several washing steps at 37°C in a low buffer concentration, and remains stable). Moderately stringent conditions, as defined herein, involve including washing in 3x SSC at 42°C, or the art-recognized equivalent thereof. The parameters of salt concentration and temperature can be varied to achieve the optimal level of identity between the probe and the target nucleic acid. Guidance regarding such conditions is available in the art, for example, by Sambrook et al., 1989, Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, N.Y.; and Ausubel et al. (eds.), 1995, Current Protocols in Molecular Biology, (John Wiley & Sons, N.Y.) at Unit 2.10.

Overview:

The present invention provides for molecular genetic markers that have novel utility for the analysis of methylation patterns associated with the development of prostate cell proliferative disorders. Said markers may be used for detecting and/or distinguishing between prostate cell proliferative disorders, thereby providing improved means for the classification and treatment of said disorders. It is particularly preferred that the markers according to the invention be used as the basis for a diagnostic test to be used for prostate cancer, to be used as an alternative or adjunct test to current tests. In one embodiment of the method, such a diagnostic test may be used post PSA screening of individuals with elevated PSA levels.

Bisulfite modification of DNA is an art-recognized tool used to assess CpG methylation status. 5-methylcytosine is the most frequent covalent base modification in the DNA of eukaryotic cells. It plays a role, for example, in the regulation of the transcription, in genetic imprinting, and in tumorigenesis. Therefore, the identification of 5-methylcytosine as a component of genetic information is of considerable interest. However, 5-methylcytosine positions cannot be identified by sequencing, because 5-methylcytosine has the same base

pairing behavior as cytosine. Moreover, the epigenetic information carried by 5-methylcytosine is completely lost during, *e.g.*, PCR amplification.

The most frequently used method for analyzing DNA for the presence of 5-methylcytosine is based upon the specific reaction of bisulfite with cytosine whereby, upon subsequent alkaline hydrolysis, cytosine is converted to uracil which corresponds to thymine in its base pairing behavior. Significantly, however, 5-methylcytosine remains unmodified under these conditions. Consequently, the original DNA is *converted* in such a manner that methylcytosine, which originally could not be distinguished from cytosine by its hybridization behavior, can now be detected as the only remaining cytosine using standard, art-recognized molecular biological techniques, for example, by amplification and hybridization, or by sequencing. All of these techniques are based on differential base pairing properties, which can now be fully exploited.

The prior art, in terms of sensitivity, is defined by a method comprising enclosing the DNA to be analyzed in an agarose matrix, thereby preventing the diffusion and renaturation of the DNA (bisulfite only reacts with single-stranded DNA), and replacing all precipitation and purification steps with fast dialysis (Olek A, et al., A modified and improved method for bisulfite based cytosine methylation analysis, *Nucleic Acids Res.* 24:5064-6, 1996). It is thus possible to analyze individual cells for methylation status, illustrating the utility and sensitivity of the method. An overview of art-recognized methods for detecting 5-methylcytosine is provided by Rein, T., et al., *Nucleic Acids Res.*, 26:2255, 1998.

The bisulfite technique, barring few exceptions (*e.g.*, Zeschnigk M, et al., *Eur J Hum Genet.* 5:94-98, 1997), is currently only used in research. In all instances, short, specific fragments of a known gene are amplified subsequent to a bisulfite treatment, and either completely sequenced (Olek & Walter, *Nat Genet.* 1997 17:275-6, 1997), subjected to one or more primer extension reactions (Gonzalgo & Jones, *Nucleic Acids Res.*, 25:2529-31, 1997; WO 95/00669; U.S. Patent No. 6,251,594) to analyze individual cytosine positions, or treated by enzymatic digestion (Xiong & Laird, *Nucleic Acids Res.*, 25:2532-4, 1997). Detection by hybridization has also been described in the art (Olek et al., WO 99/28498). Additionally, use of the bisulfite technique for methylation detection with respect to individual genes has been described (Grigg & Clark, *Bioessays*, 16:431-6, 1994; Zeschnigk M, et al., *Hum Mol Genet.*, 6:387-95, 1997; Feil R, et al., *Nucleic Acids Res.*, 22:695-, 1994; Martin V, et al., *Gene*, 157:261-4, 1995; WO 9746705 and WO 9515373).

The present invention provides for the use of the bisulfite technique, in combination with one or more methylation assays, for determination of the methylation status of CpG

dinucleotide sequences within sequences from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 59 . According to the present invention, determination of the methylation status of CpG dinucleotide sequences within sequences from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 59 has diagnostic and prognostic utility.

Methylation Assay Procedures. Various methylation assay procedures are known in the art, and can be used in conjunction with the present invention. These assays allow for determination of the methylation state of one or a plurality of CpG dinucleotides (*e.g.*, CpG islands) within a DNA sequence. Such assays involve, among other techniques, DNA sequencing of bisulfite-treated DNA, PCR (for sequence-specific amplification), Southern blot analysis, and use of methylation-sensitive restriction enzymes.

For example, genomic sequencing has been simplified for analysis of DNA methylation patterns and 5-methylcytosine distribution by using bisulfite treatment (Frommer et al., *Proc. Natl. Acad. Sci. USA* 89:1827-1831, 1992). Additionally, restriction enzyme digestion of PCR products amplified from bisulfite-converted DNA is used, *e.g.*, the method described by Sadri & Hornsby (*Nucl. Acids Res.* 24:5058-5059, 1996), or COBRA (Combined Bisulfite Restriction Analysis) (Xiong & Laird, *Nucleic Acids Res.* 25:2532-2534, 1997).

COBRA. COBRA analysis is a quantitative methylation assay useful for determining DNA methylation levels at specific gene loci in small amounts of genomic DNA (Xiong & Laird, *Nucleic Acids Res.* 25:2532-2534, 1997). Briefly, restriction enzyme digestion is used to reveal methylation-dependent sequence differences in PCR products of sodium bisulfite-treated DNA. Methylation-dependent sequence differences are first introduced into the genomic DNA by standard bisulfite treatment according to the procedure described by Frommer et al. (*Proc. Natl. Acad. Sci. USA* 89:1827-1831, 1992). PCR amplification of the bisulfite converted DNA is then performed using primers specific for the interested CpG islands, followed by restriction endonuclease digestion, gel electrophoresis, and detection using specific, labeled hybridization probes. Methylation levels in the original DNA sample are represented by the relative amounts of digested and undigested PCR product in a linearly quantitative fashion across a wide spectrum of DNA methylation levels. In addition, this technique can be reliably applied to DNA obtained from microdissected paraffin-embedded tissue samples. Typical reagents (*e.g.*, as might be found in a typical COBRA-based kit) for COBRA analysis may include, but are not limited to: PCR primers for specific gene (or methylation-altered DNA sequence or CpG island); restriction enzyme and appropriate buffer; gene-hybridization oligo; control hybridization oligo; kinase labeling kit for oligo probe; and

radioactive nucleotides. Additionally, bisulfite conversion reagents may include: DNA denaturation buffer; sulfonation buffer; DNA recovery reagents or kits (*e.g.*, precipitation, ultrafiltration, affinity column); desulfonation buffer; and DNA recovery components.

Preferably, assays such as "MethyLight™" (a fluorescence-based real-time PCR technique) (Eads et al., *Cancer Res.* 59:2302-2306, 1999), Ms-SNuPE (Methylation-sensitive Single Nucleotide Primer Extension) reactions (Gonzalgo & Jones, *Nucleic Acids Res.* 25:2529-2531, 1997), methylation-specific PCR ("MSP"; Herman et al., *Proc. Natl. Acad. Sci. USA* 93:9821-9826, 1996; US Patent No. 5,786,146), and methylated CpG island amplification ("MCA"; Toyota et al., *Cancer Res.* 59:2307-12, 1999) are used alone or in combination with other of these methods.

MethyLight™. The MethyLight™ assay is a high-throughput quantitative methylation assay that utilizes fluorescence-based real-time PCR (TaqMan®) technology that requires no further manipulations after the PCR step (Eads et al., *Cancer Res.* 59:2302-2306, 1999). Briefly, the MethyLight™ process begins with a mixed sample of genomic DNA that is converted, in a sodium bisulfite reaction, to a mixed pool of methylation-dependent sequence differences according to standard procedures (the bisulfite process converts unmethylated cytosine residues to uracil). Fluorescence-based PCR is then performed either in an "unbiased" (with primers that do not overlap known CpG methylation sites) PCR reaction, or in a "biased" (with PCR primers that overlap known CpG dinucleotides) reaction. Sequence discrimination can occur either at the level of the amplification process or at the level of the fluorescence detection process, or both.

The MethyLight™ assay may be used as a quantitative test for methylation patterns in the genomic DNA sample, wherein sequence discrimination occurs at the level of probe hybridization. In this quantitative version, the PCR reaction provides for unbiased amplification in the presence of a fluorescent probe that overlaps a particular putative methylation site. An unbiased control for the amount of input DNA is provided by a reaction in which neither the primers, nor the probe overlie any CpG dinucleotides. Alternatively, a qualitative test for genomic methylation is achieved by probing of the biased PCR pool with either control oligonucleotides that do not "cover" known methylation sites (a fluorescence-based version of the "MSP" technique), or with oligonucleotides covering potential methylation sites.

The MethyLight™ process can by used with a "TaqMan®" probe in the amplification process. For example, double-stranded genomic DNA is treated with sodium bisulfite and subjected to one of two sets of PCR reactions using TaqMan® probes; *e.g.*, with either biased

primers and TaqMan® probe, or unbiased primers and TaqMan® probe. The TaqMan® probe is dual-labeled with fluorescent "reporter" and "quencher" molecules, and is designed to be specific for a relatively high GC content region so that it melts out at about 10°C higher temperature in the PCR cycle than the forward or reverse primers. This allows the TaqMan® probe to remain fully hybridized during the PCR annealing/extension step. As the Taq polymerase enzymatically synthesizes a new strand during PCR, it will eventually reach the annealed TaqMan® probe. The Taq polymerase 5' to 3' endonuclease activity will then displace the TaqMan® probe by digesting it to release the fluorescent reporter molecule for quantitative detection of its now unquenched signal using a real-time fluorescent detection system.

Typical reagents (*e.g.*, as might be found in a typical MethyLight™-based kit) for MethyLight™ analysis may include, but are not limited to: PCR primers for specific gene (or methylation-altered DNA sequence or CpG island); TaqMan® probes; optimized PCR buffers and deoxynucleotides; and Taq polymerase.

Ms-SNuPE. The Ms-SNuPE technique is a quantitative method for assessing methylation differences at specific CpG sites based on bisulfite treatment of DNA, followed by single-nucleotide primer extension (Gonzalgo & Jones, *Nucleic Acids Res.* 25:2529-2531, 1997). Briefly, genomic DNA is reacted with sodium bisulfite to convert unmethylated cytosine to uracil while leaving 5-methylcytosine unchanged. Amplification of the desired target sequence is then performed using PCR primers specific for bisulfite-converted DNA, and the resulting product is isolated and used as a template for methylation analysis at the CpG site(s) of interest. Small amounts of DNA can be analyzed (*e.g.*, microdissected pathology sections), and it avoids utilization of restriction enzymes for determining the methylation status at CpG sites.

Typical reagents (*e.g.*, as might be found in a typical Ms-SNuPE-based kit) for Ms-SNuPE analysis may include, but are not limited to: PCR primers for specific gene (or methylation-altered DNA sequence or CpG island); optimized PCR buffers and deoxynucleotides; gel extraction kit; positive control primers; Ms-SNuPE primers for specific gene; reaction buffer (for the Ms-SNuPE reaction); and radioactive nucleotides. Additionally, bisulfite conversion reagents may include: DNA denaturation buffer; sulfonation buffer; DNA recovery regents or kit (*e.g.*, precipitation, ultrafiltration, affinity column); desulfonation buffer; and DNA recovery components.

MSP. MSP (methylation-specific PCR) allows for assessing the methylation status of virtually any group of CpG sites within a CpG island, independent of the use of methylation-

sensitive restriction enzymes (Herman et al. *Proc. Natl. Acad. Sci. USA* 93:9821-9826, 1996; US Patent No. 5,786,146). Briefly, DNA is modified by sodium bisulfite which convertsall unmethylated, but not methylated cytosines to uracil. DNA can subsequently be amplified with primers specific for methylated versus unmethylated DNA. MSP requires only small quantities of DNA, is sensitive to 0.1% methylated alleles of a given CpG island locus, and can be performed on DNA extracted from paraffin-embedded samples. Typical reagents (*e.g.*, as might be found in a typical MSP-based kit) for MSP analysis may include, but are not limited to: methylated and unmethylated PCR primers for specific gene (or methylation-altered DNA sequence or CpG island), optimized PCR buffers and deoxynucleotides, and specific probes.

MCA. The MCA technique is a method that can be used to screen for altered methylation patterns in genomic DNA, and to isolate specific sequences associated with these changes (Toyota et al., *Cancer Res.* 59:2307-12, 1999). Briefly, restriction enzymes with different sensitivities to cytosine methylation in their recognition sites are used to digest genomic DNAs from primary tumors, cell lines, and normal tissues prior to arbitrarily primed PCR amplification. Fragments that show differential methylation are cloned and sequenced after resolving the PCR products on high-resolution polyacrylamide gels. The cloned fragments are then used as probes for Southern analysis to confirm differential methylation of these regions. Typical reagents (*e.g.*, as might be found in a typical MCA-based kit) for MCA analysis may include, but are not limited to: PCR primers for arbitrary priming Genomic DNA; PCR buffers and nucleotides, restriction enzymes and appropriate buffers; gene-hybridization oligos or probes; control hybridization oligos or probes.

HeavyMethyl. The HeavyMethyl technique is a means for selectively amplifying methylated as opposed to non-methylated DNA (or vice versa). Blocker oligonucleotides specific to either methylated or unmenthylated versions of a bisulfite treated target sequence are hybridised to the treated nucleic acids. The sample is then enzymatically amplified, wherein the hybridisation of the blocker oligonucleotides hinders amplification of the nucleic acid strand to which it is bound. Typical reagents (*e.g.*, as might be found in a typical HeavyMethyl-based kit) for HeavyMethyl analysis may include, but are not limited to: methylated or unmethylated blocker oligonucleotides for specific gene (or methylation-altered DNA sequence or CpG island), optimized PCR buffers and deoxynucleotides, and specific probes and primers.

GENOMIC SEQUENCES ACCORDING TO SEQ ID NO: 1 to SEQ ID NO: 59 , AND TREATED VARIANTS THEREOF ACCORDING TO SEQ ID NO: 60 to SEQ ID NO: 295, WERE DETERMINED TO HAVE UTILITY FOR THE DETECTION AND/OR CLASSIFICATION OF PROSTATE CELL PROLIFERATIVE DISORDERS.

The present invention is based upon the analysis of methylation levels within one or more genomic sequences taken from the group consisting SEQ ID NO: 1 to SEQ ID NO: 59 .

Particular embodiments of the present invention provide a novel application of the analysis of methylation levels and/or patterns within said sequences that enables a precise detection and/or classification of prostate cell proliferative disorders. Early detection of prostate cell proliferative disorders is directly linked with disease prognosis, and the disclosed method thereby enables the physician and patient to make better and more informed treatment decisions.

FURTHER IMPROVEMENTS

The present invention provides novel uses for genomic sequences selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 59 . Additional embodiments provide modified variants of SEQ ID NO: 1 to SEQ ID NO: 59 , as well as oligonucleotides and/or PNA-oligomers for analysis of cytosine methylation patterns within SEQ ID NO: 1 to SEQ ID NO: 59 .

An objective of the invention comprises analysis of the methylation state of one or more CpG dinucleotides within at least one of the genomic sequences selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 59 and sequences complementary thereto.

The disclosed invention provides treated nucleic acids, derived from genomic SEQ ID NO: 1 to SEQ ID NO 59, wherein the treatment is suitable to convert at least one unmethylated cytosine base of the genomic DNA sequence to uracil or another base that is detectably dissimilar to cytosine in terms of hybridization. The genomic sequences in question may comprise one, or more, consecutive or random methylated CpG positions. Said treatment preferrably comprises use of a reagent selected from the group consisting of bisulfite, hydrogen sulfite, disulfite, and combinations thereof. In a preferred embodiment of the invention, the objective comprises analysis of a modified nucleic acid comprising a sequence of at least 16 contiguous nucleotide bases in length of a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and preferably wherein said sequence comprises at least one CpG, TpA or CpA dinucleotide and sequences complementary thereto. The sequences of SEQ ID NO: 60 to SEQ ID NO: 295 provide modified versions of the

nucleic acid according to SEQ ID NO: 1 to SEQ ID NO: 59 , wherein the modification of each genomic sequence results in the synthesis of a nucleic acid having a sequence that is unique and distinct from said genomic sequence as follows. For each sense strand genomic DNA, e.g., SEQ ID NO:1, four converted versions are disclosed. A first version wherein "C" →"T," but "CpG" remains "CpG" (*i.e.*, corresponds to case where, for the genomic sequence, all "C" residues of CpG dinucleotide sequences are methylated and are thus not converted). For each genomic sequence SEQ ID NO:1 to SEQ ID NO:59) the equivalent sequence can be identified as SEQ ID NO. = 60 + (X-1)2, wherein X = SEQ ID NO. of the genomic sequence. Therefore, the pretreated equivalent sequence to SEQ ID NO:1 is SEQ ID NO:60, the equivalent sequence to SEQ ID NO:2 is SEQ ID NO: 62 and the equivalent sequence to SEQ ID NO:3 is SEQ ID NO: 64. A second version discloses the complement of the disclosed genomic DNA sequence (i.e. *anti*sense strand), wherein "C"→"T," but "CpG" remains "CpG" (*i.e.*, corresponds to case where, for all "C" residues of CpG dinucleotide sequences are methylated and are thus not converted). For each genomic sequence SEQ ID NO:1 to SEQ ID NO:59) the equivalent sequence can be identified as SEQ ID NO. = 61 + (X-1)2, wherein X = SEQ ID NO. of the genomic sequence. Therefore, the pretreated equivalent sequence to SEQ ID NO:1 is SEQ ID NO:61, the equivalent sequence to SEQ ID NO:2 is SEQ ID NO: 63 and the equivalent sequence to SEQ ID NO:3 is SEQ ID NO: 65. The 'upmethylated' converted sequences of SEQ ID NO: 1 to SEQ ID NO: 59 correspond to SEQ ID NO: 60 to SEQ ID NO: 177. A third chemically converted version of each genomic sequences is provided, wherein "C"→"T" for all "C" residues, including those of "CpG" dinucleotide sequences (*i.e.*, corresponds to case where, for the genomic sequences, all "C" residues of CpG dinucleotide sequences are <u>un</u>methylated). For each genomic sequence SEQ ID NO:1 to SEQ ID NO:59) the equivalent sequence can be identified as SEQ ID NO. = 178 + (X-1)2, wherein X = SEQ ID NO. of the genomic sequence. Therefore, the pretreated equivalent sequence to SEQ ID NO:1 is SEQ ID NO:178, the equivalent sequence to SEQ ID NO:2 is SEQ ID NO: 180 and the equivalent sequence to SEQ ID NO:3 is SEQ ID NO: 182. A final chemically converted version of each sequence, discloses the complement of the disclosed genomic DNA sequence (i.e. *anti*sense strand), wherein "C"→"T" for all "C" residues, including those of "CpG" dinucleotide sequences (*i.e.*, corresponds to case where, for the complement (*anti*sense strand) of each genomic sequence, all "C" residues of CpG dinucleotide sequences are <u>un</u>methylated). For each genomic sequence SEQ ID NO:1 to SEQ ID NO:59) the equivalent sequence can be identified as SEQ ID NO. = 179 + (X-1)2, wherein X = SEQ ID NO. of the genomic sequence. Therefore, the pretreated equivalent sequence to

SEQ ID NO:1 is SEQ ID NO:179, the equivalent sequence to SEQ ID NO:2 is SEQ ID NO: 181 and the equivalent sequence to SEQ ID NO:3 is SEQ ID NO: 183. The 'downmethylated' converted sequences of SEQ ID NO: 1 to SEQ ID NO: 59 correspond to SEQ ID NO: 177 to SEQ ID NO: 295. Further descriptions of the genomic sequences are in Table 8, including, in some cases, gene names. In some cases, the sequences are not within coding regions of genes and gene names have therefore not been given.

In an alternative preferred embodiment, such analysis comprises the use of an oligonucleotide or oligomer for detecting the cytosine methylation state within genomic or pretreated (chemically modified) DNA, according to SEQ ID NO: 1 to SEQ ID NO: 295. Said oligonucleotide or oligomer comprising a nucleic acid sequence having a length of at least nine (9) nucleotides which hybridizes, under moderately stringent or stringent conditions (as defined herein above), to a pretreated nucleic acid sequence according to SEQ ID NO: 60 to SEQ ID NO: 295 and/or sequences complementary thereto, or to a genomic sequence according to SEQ ID NO: 1 to SEQ ID NO: 59 and/or sequences complementary thereto.

Thus, the present invention includes nucleic acid molecules (*e.g.*, oligonucleotides and peptide nucleic acid (PNA) molecules (PNA-oligomers)) that hybridize under moderately stringent and/or stringent hybridization conditions to all or a portion of the sequences SEQ ID NO: 1 to SEQ ID NO: 295, or to the complements thereof. The hybridizing portion of the hybridizing nucleic acids is typically at least 9, 15, 20, 25, 30 or 35 nucleotides in length. However, longer molecules have inventive utility, and are thus within the scope of the present invention.

Preferably, the hybridizing portion of the inventive hybridizing nucleic acids is at least 95%, or at least 98%, or 100% identical to the sequence, or to a portion thereof of SEQ ID NO: 1 to SEQ ID NO: 295, or to the complements thereof.

Hybridizing nucleic acids of the type described herein can be used, for example, as a primer (*e.g.*, a PCR primer), or a diagnostic and/or prognostic probe or primer. Preferably, hybridization of the oligonucleotide probe to a nucleic acid sample is performed under stringent conditions and the probe is 100% identical to the target sequence. Nucleic acid duplex or hybrid stability is expressed as the melting temperature or Tm, which is the temperature at which a probe dissociates from a target DNA. This melting temperature is used to define the required stringency conditions.

For target sequences that are related and substantially identical to the corresponding sequence of SEQ ID NO: 1 to SEQ ID NO: 59 (such as allelic variants and SNPs), rather than

identical, it is useful to first establish the lowest temperature at which only homologous hybridization occurs with a particular concentration of salt (*e.g.*, SSC or SSPE). Then, assuming that 1% mismatching results in a 1°C decrease in the Tm, the temperature of the final wash in the hybridization reaction is reduced accordingly (for example, if sequences having > 95% identity with the probe are sought, the final wash temperature is decreased by 5°C). In practice, the change in Tm can be between 0.5°C and 1.5°C per 1% mismatch.

Examples of inventive oligonucleotides of length X (in nucleotides), as indicated by polynucleotide positions with reference to, *e.g.*, SEQ ID NO:1, include those corresponding to sets (sense and antisense sets) of consecutively overlapping oligonucleotides of length X, where the oligonucleotides within each consecutively overlapping set (corresponding to a given X value) are defined as the finite set of Z oligonucleotides from nucleotide positions:

n to (n + (X-1));

where n=1, 2, 3,...(Y-(X-1));

where Y equals 2299 base pairs.

where X equals the common length (in nucleotides) of each oligonucleotide in the set (*e.g.*, X=20 for a set of consecutively overlapping 20-mers); and

where the number (Z) of consecutively overlapping oligomers of length X for a given SEQ ID NO of length Y is equal to Y-(X-1).

Preferably, the set is limited to those oligomers that comprise at least one CpG, TpG or CpA dinucleotide.

Examples of inventive 20-mer oligonucleotides include the following set of 2299 oligomers (and the antisense set complementary thereto), indicated by polynucleotide positions with reference to SEQ ID NO:1 1-20, 2-21, 3-22, 4-23, 5-24, ...
Preferably, the set is limited to those oligomers that comprise at least one CpG, TpG or CpA dinucleotide.

The present invention encompasses, for *each* of SEQ ID NO: 1 to SEQ ID NO: 295 (sense and antisense), multiple consecutively overlapping sets of oligonucleotides or modified oligonucleotides of length X, where, *e.g.*, X= 9, 10, 17, 20, 22, 23, 25, 27, 30 or 35 nucleotides.

The oligonucleotides or oligomers according to the present invention constitute effective tools useful to ascertain genetic and epigenetic parameters of the genomic sequence corresponding to SEQ ID NO: 1 to SEQ ID NO: 59 . Preferred sets of such oligonucleotides or modified oligonucleotides of length X are those consecutively overlapping sets of

oligomers corresponding to SEQ ID NO: 1 to SEQ ID NO: 295 (and to the complements thereof). Preferably, said oligomers comprise at least one CpG, TpG or CpA dinucleotide.

Particularly preferred oligonucleotides or oligomers according to the present invention are those in which the cytosine of the CpG dinucleotide (or of the corresponding converted TpG or CpA dinculeotide) sequences is within the middle third of the oligonucleotide; that is, where the oligonucleotide is, for example, 13 bases in length, the CpG, TpG or CpA dinucleotide is positioned within the fifth to ninth nucleotide from the 5'-end.

The oligonucleotides of the invention can also be modified by chemically linking the oligonucleotide to one or more moieties or conjugates to enhance the activity, stability or detection of the oligonucleotide. Such moieties or conjugates include chromophores, fluorophors, lipids such as cholesterol, cholic acid, thioether, aliphatic chains, phospholipids, polyamines, polyethylene glycol (PEG), palmityl moieties, and others as disclosed in, for example, United States Patent Numbers 5,514,758, 5,565,552, 5,567,810, 5,574,142, 5,585,481, 5,587,371, 5,597,696 and 5,958,773. The probes may also exist in the form of a PNA (peptide nucleic acid) which has particularly preferred pairing properties. Thus, the oligonucleotide may include other appended groups such as peptides, and may include hybridization-triggered cleavage agents (Krol et al., *BioTechniques* 6:958-976, 1988) or intercalating agents (Zon, *Pharm. Res.* 5:539-549, 1988). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a chromophore, fluorophor, peptide, hybridization-triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

The oligonucleotide may also comprise at least one art-recognized modified sugar and/or base moiety, or may comprise a modified backbone or non-natural internucleoside linkage.

The oligonucleotides or oligomers according to particular embodiments of the present invention are typically used in 'sets,' which contain at least one oligomer for analysis of each of the CpG dinucleotides of genomic sequence SEQ ID NO: 1 to SEQ ID NO: 59 and sequences complementary thereto, or to the corresponding CpG, TpG or CpA dinucleotide within a sequence of the pretreated nucleic acids according to SEQ ID NO: 60 to SEQ ID NO: 295 and sequences complementary thereto. However, it is anticipated that for economic or other factors it may be preferable to analyze a limited selection of the CpG dinucleotides within said sequences, and the content of the set of oligonucleotides is altered accordingly.

Therefore, in particular embodiments, the present invention provides a set of at least two (2) (oligonucleotides and/or PNA-oligomers) useful for detecting the cytosine

methylation state in pretreated genomic DNA (SEQ ID NO: 60 to SEQ ID NO: 295), or in genomic DNA (SEQ ID NO: 1 to SEQ ID NO: 59 and sequences complementary thereto). These probes enable detection and/or classification of genetic and epigenetic parameters of prostate cell proliferative disorders. The set of oligomers may also be used for detecting single nucleotide polymorphisms (SNPs) in pretreated genomic DNA (SEQ ID NO: 60 to SEQ ID NO: 295), or in genomic DNA (SEQ ID NO: 1 to SEQ ID NO: 59 and sequences complementary thereto).

In preferred embodiments, at least one, and more preferably all members of a set of oligonucleotides is bound to a solid phase.

In further embodiments, the present invention provides a set of at least two (2) oligonucleotides that are used as 'primer' oligonucleotides for amplifying DNA sequences of one of SEQ ID NO: 1 to SEQ ID NO: 295 and sequences complementary thereto, or segments thereof.

It is anticipated that the oligonucleotides may constitute all or part of an "array" or "DNA chip" (*i.e.*, an arrangement of different oligonucleotides and/or PNA-oligomers bound to a solid phase). Such an array of different oligonucleotide- and/or PNA-oligomer sequences can be characterized, for example, in that it is arranged on the solid phase in the form of a rectangular or hexagonal lattice. The solid-phase surface may be composed of silicon, glass, polystyrene, aluminum, steel, iron, copper, nickel, silver, or gold. Nitrocellulose as well as plastics such as nylon, which can exist in the form of pellets or also as resin matrices, may also be used. An overview of the Prior Art in oligomer array manufacturing can be gathered from a special edition of Nature Genetics (*Nature Genetics Supplement*, Volume 21, January 1999, and from the literature cited therein). Fluorescently labeled probes are often used for the scanning of immobilized DNA arrays. The simple attachment of Cy3 and Cy5 dyes to the 5'-OH of the specific probe are particularly suitable for fluorescence labels. The detection of the fluorescence of the hybridized probes may be carried out, for example, via a confocal microscope. Cy3 and Cy5 dyes, besides many others, are commercially available.

It is particularly preferred that the oligomers according to the invention are utilised for at least one of: detection of; detection and differentiation between or among subclasses of; diagnosis of; prognosis of; treatment of; monitoring of; and treatment and monitoring of prostate cell proliferative disorders. This is enabled by use of said sets for the detection or detection and differentiation of prostate cell proliferative disorders.

The present invention further provides a method for ascertaining genetic and/or epigenetic parameters of the genomic sequences according to SEQ ID NO: 1 to SEQ ID NO:

59 within a subject by analyzing cytosine methylation and single nucleotide polymorphisms. Said method comprising contacting a nucleic acid comprising one or more of SEQ ID NO: 1 to SEQ ID NO: 59 in a biological sample obtained from said subject with at least one reagent or a series of reagents, wherein said reagent or series of reagents, distinguishes between methylated and non-methylated CpG dinucleotides within the target nucleic acid.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that said nucleotide sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that said nucleotide sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that said nucleotide sequence(s) comprise, or hybridizes to, one or more more sequences comprising at least 16 contiguous nucleotides of the sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Preferably, said method comprises the following steps: In the *first step*, a sample of the tissue to be analysed is obtained. The source may be any suitable source, such as cell lines, histological slides, biopsies, tissue embedded in paraffin, bodily fluids, ejaculate, urine, blood and all possible combinations thereof. In a particularly preferred embodiment of the method said source is bodily fluids including post prostatic massage urine, ejaculate, urine, or blood. The DNA is then isolated from the sample. Extraction may be by means that are standard to one skilled in the art, including the use of commercially available kits, detergent lysates, sonification and vortexing with glass beads. Briefly, wherein the DNA of interest is encapsulated by a cellular membrane the biological sample must be disrupted and lysed by enzymatic, chemical or mechanical means. The DNA solution may then be cleared of proteins and other contaminants e.g. by digestion with proteinase K. The genomic DNA is then recovered from the solution. This may be carried out by means of a variety of methods including salting out, organic extraction or binding of the DNA to a solid phase support. The

choice of method will be affected by several factors including time, expense and required quantity of DNA.

Once the nucleic acids have been extracted, the genomic double stranded DNA is used in the analysis.

In the *second step* of the method, the genomic DNA sample is treated in such a manner that cytosine bases which are unmethylated at the 5'-position are converted to uracil, thymine, or another base which is dissimilar to cytosine in terms of hybridization behavior. This will be understood as 'pretreatment' herein.

The above-described treatment of genomic DNA is preferably carried out with bisulfite (hydrogen sulfite, disulfite) and subsequent alkaline hydrolysis that results in a conversion of non-methylated cytosine nucleobases to uracil or to another base that is dissimilar to cytosine in terms of base pairing behavior.

In the *third step* of the method, fragments of the pretreated DNA are amplified, using sets of primer oligonucleotides according to the present invention, and an amplification enzyme. The amplification of several DNA segments can be carried out simultaneously in one and the same reaction vessel. Typically, the amplification is carried out using a polymerase chain reaction (PCR). The set of primer oligonucleotides includes at least two oligonucleotides whose sequences are each reverse complementary, identical, or hybridize under stringent or highly stringent conditions to an at least 16-base-pair long segment of the base sequences of one or more of SEQ ID NO: 60 to SEQ ID NO: 295 and sequences complementary thereto.

In an alternate embodiment of the method, the methylation status of preselected CpG positions within the nucleic acid sequences comprising one or more of SEQ ID NO: 1 to SEQ ID NO: 59 may be detected by use of methylation-specific primer oligonucleotides. This technique (MSP) has been described in United States Patent No. 6,265,171 to Herman. The use of methylation status specific primers for the amplification of bisulfite treated DNA allows the differentiation between methylated and unmethylated nucleic acids. MSP primers pairs contain at least one primer that hybridizes to a bisulfite treated CpG dinucleotide. Therefore, the sequence of said primers comprises at least one CpG dinucleotide. MSP primers specific for non-methylated DNA contain a "T' at the 3' position of the C position in the CpG. Preferably, therefore, the base sequence of said primers is required to comprise a sequence having a length of at least 9 nucleotides which hybridizes to a pretreated nucleic acid sequence according to one of SEQ ID NO: 60 to SEQ ID NO: 295 and sequences

complementary thereto, wherein the base sequence of said oligomers comprises at least one CpG dinucleotide.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that said nucleotide sequence(s) hybridizes to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that said nucleotide sequence(s) hybridizes to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that said nucleotide sequence(s) hybridizes to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

A further preferred embodiment of the method comprises the use of *blocker* oligonucleotides. The use of such blocker oligonucleotides has been described by Yu et al., *BioTechniques* 23:714-720, 1997. Blocking probe oligonucleotides are hybridized to the bisulfite treated nucleic acid concurrently with the PCR primers. PCR amplification of the nucleic acid is terminated at the 5' position of the blocking probe, such that amplification of a nucleic acid is suppressed where the complementary sequence to the blocking probe is present. The probes may be designed to hybridize to the bisulfite treated nucleic acid in a methylation status specific manner. For example, for detection of methylated nucleic acids within a population of unmethylated nucleic acids, suppression of the amplification of nucleic acids which are unmethylated at the position in question would be carried out by the use of blocking probes comprising a 'CpA' or 'TpA' at the position in question, as opposed to a 'CpG' if the suppression of amplification of methylated nucleic acids is desired.

For PCR methods using blocker oligonucleotides, efficient disruption of polymerase-mediated amplification requires that blocker oligonucleotides not be elongated by the polymerase. Preferably, this is achieved through the use of blockers that are 3'-deoxyoligonucleotides, or oligonucleotides derivitized at the 3' position with other than a "free" hydroxyl group. For example, 3'-O-acetyl oligonucleotides are representative of a preferred class of blocker molecule.

Additionally, polymerase-mediated decomposition of the blocker oligonucleotides should be precluded. Preferably, such preclusion comprises either use of a polymerase lacking 5'-3' exonuclease activity, or use of modified blocker oligonucleotides having, for example, thioate bridges at the 5'-terminii thereof that render the blocker molecule nuclease-resistant. Particular applications may not require such 5' modifications of the blocker. For example, if the blocker- and primer-binding sites overlap, thereby precluding binding of the primer (*e.g.*, with excess blocker), degradation of the blocker oligonucleotide will be substantially precluded. This is because the polymerase will not extend the primer toward, and through (in the 5'-3' direction) the blocker—a process that normally results in degradation of the hybridized blocker oligonucleotide.

A particularly preferred blocker/PCR embodiment, for purposes of the present invention and as implemented herein, comprises the use of peptide nucleic acid (PNA) oligomers as blocking oligonucleotides. Such PNA blocker oligomers are ideally suited, because they are neither decomposed nor extended by the polymerase.

Preferably, therefore, the base sequence of said *blocking oligonucleotides* is required to comprise a sequence having a length of at least 9 nucleotides which hybridizes to a pretreated nucleic acid sequence according to one of SEQ ID NO: 60 to SEQ ID NO: 295 and sequences complementary thereto, wherein the base sequence of said oligonucleotides comprises at least one CpG, TpG or CpA dinucleotide.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that said *blocking oligonucleotide* nucleotide sequence(s) hybridizes to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that said *blocking oligonucleotide* nucleotide sequence(s) hybridizes to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that said *blocking oligonucleotide* nucleotide sequence(s) hybridizes to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

The fragments obtained by means of the amplification can carry a directly or indirectly detectable label. Preferred are labels in the form of fluorescence labels, radionuclides, or detachable molecule fragments having a typical mass that can be detected in a mass spectrometer. Where said labels are mass labels, it is preferred that the labeled amplificates have a single positive or negative net charge, allowing for better detectability in the mass spectrometer. The detection may be carried out and visualized by means of, *e.g.*, matrix assisted laser desorption/ionization mass spectrometry (MALDI) or using electron spray mass spectrometry (ESI).

Matrix Assisted Laser Desorption/Ionization Mass Spectrometry (MALDI-TOF) is a very efficient development for the analysis of biomolecules (Karas & Hillenkamp, *Anal Chem.*, 60:2299-301, 1988). An analyte is embedded in a light-absorbing matrix. The matrix is evaporated by a short laser pulse thus transporting the analyte molecule into the vapour phase in an unfragmented manner. The analyte is ionized by collisions with matrix molecules. An applied voltage accelerates the ions into a field-free flight tube. Due to their different masses, the ions are accelerated at different rates. Smaller ions reach the detector sooner than bigger ones. MALDI-TOF spectrometry is well suited to the analysis of peptides and proteins. The analysis of nucleic acids is somewhat more difficult (Gut & Beck, *Current Innovations and Future Trends*, 1:147-57, 1995). The sensitivity with respect to nucleic acid analysis is approximately 100-times less than for peptides, and decreases disproportionally with increasing fragment size. Moreover, for nucleic acids having a multiply negatively charged backbone, the ionization process via the matrix is considerably less efficient. In MALDI-TOF spectrometry, the selection of the matrix plays an eminently important role. For desorption of peptides, several very efficient matrixes have been found which produce a very fine crystallisation. There are now several responsive matrixes for DNA, however, the difference in sensitivity between peptides and nucleic acids has not been reduced. This difference in sensitivity can be reduced, however, by chemically modifying the DNA in such a manner that it becomes more similar to a peptide. For example, phosphorothioate nucleic acids, in which the usual phosphates of the backbone are substituted with thiophosphates, can be converted into a charge-neutral DNA using simple alkylation chemistry (Gut & Beck, *Nucleic Acids Res.* 23: 1367-73, 1995). The coupling of a charge tag to this modified DNA results in an increase in MALDI-TOF sensitivity to the same level as that found for peptides. A further advantage of charge tagging is the increased stability of the analysis against impurities, which makes the detection of unmodified substrates considerably more difficult.

In the *fourth step* of the method, the amplificates obtained during the third step of the method are analysed in order to ascertain the methylation status of the CpG dinucleotides prior to the treatment.

In embodiments where the amplificates were obtained by means of MSP amplification, the presence or absence of an amplificate is in itself indicative of the methylation state of the CpG positions covered by the primer, according to the base sequences of said primer.

Amplificates obtained by means of both standard and methylation specific PCR may be further analyzed by means of hybridization-based methods such as, but not limited to, array technology and probe based technologies as well as by means of techniques such as sequencing and template directed extension.

In one embodiment of the method, the amplificates synthesised in *step three* are subsequently hybridized to an array or a set of oligonucleotides and/or PNA probes. In this context, the hybridization takes place in the following manner: the set of probes used during the hybridization is preferably composed of at least 2 oligonucleotides or PNA-oligomers; in the process, the amplificates serve as probes which hybridize to oligonucleotides previously bonded to a solid phase; the non-hybridized fragments are subsequently removed; said oligonucleotides contain at least one base sequence having a length of at least 9 nucleotides which is reverse complementary or identical to a segment of the base sequences specified in the present Sequence Listing; and the segment comprises at least one CpG , TpG or CpA dinucleotide.

In a preferred embodiment, said dinucleotide is present in the central third of the oligomer. For example, wherein the oligomer comprises one CpG dinucleotide, said dinucleotide is preferably the fifth to ninth nucleotide from the 5'-end of a 13-mer. One oligonucleotide exists for the analysis of each CpG dinucleotide within the sequence according to SEQ ID NO: 1 to SEQ ID NO: 59 , and the equivalent positions within SEQ ID NO: 60 to SEQ ID NO: 295. Said oligonucleotides may also be present in the form of peptide nucleic acids. The non-hybridized amplificates are then removed.The hybridized amplificates are then detected. In this context, it is preferred that labels attached to the amplificates are identifiable at each position of the solid phase at which an oligonucleotide sequence is located.

In yet a further embodiment of the method, the genomic methylation status of the CpG positions may be ascertained by means of oligonucleotide probes that are hybridised to the

bisulfite treated DNA concurrently with the PCR amplification primers (wherein said primers may either be methylation specific or standard).

A particularly preferred embodiment of this method is the use of fluorescence-based Real Time Quantitative PCR (Heid et al., *Genome Res.* 6:986-994, 1996; *also see* United States Patent No. 6,331,393) employing a dual-labeled fluorescent oligonucleotide probe (TaqMan™ PCR, using an ABI Prism 7700 Sequence Detection System, Perkin Elmer Applied Biosystems, Foster City, California). The TaqMan™ PCR reaction employs the use of a nonextendible interrogating oligonucleotide, called a TaqMan™ probe, which, in preferred imbodiments, is designed to hybridize to a GpC-rich sequence located between the forward and reverse amplification primers. The TaqMan™ probe further comprises a fluorescent "reporter moiety" and a "quencher moiety" covalently bound to linker moieties (*e.g.*, phosphoramidites) attached to the nucleotides of the TaqMan™ oligonucleotide. For analysis of methylation within nucleic acids subsequent to bisulfite treatment, it is required that the probe be methylation specific, as described in United States Patent No. 6,331,393, (hereby incorporated by reference in its entirety) also known as the MethylLight™ assay. Variations on the TaqMan™ detection methodology that are also suitable for use with the described invention include the use of dual-probe technology (Lightcycler™) or fluorescent amplification primers (Sunrise™ technology). Both these techniques may be adapted in a manner suitable for use with bisulfite treated DNA, and moreover for methylation analysis within CpG dinucleotides.

A further suitable method for the use of probe oligonucleotides for the assessment of methylation by analysis of bisulfite treated nucleic acids In a further preferred embodiment of the method, the *fifth step* of the method comprises the use of template-directed oligonucleotide extension, such as MS-SNuPE as described by Gonzalgo & Jones, *Nucleic Acids Res.* 25:2529-2531, 1997.

In yet a further embodiment of the method, the *fifth step* of the method comprises sequencing and subsequent sequence analysis of the amplificate generated in the *third step* of the method (Sanger F., et al., *Proc Natl Acad Sci USA* 74:5463-5467, 1977).

In one preferred embodiment of the method the nucleic acids according to SEQ ID NO: 1 to SEQ ID NO 59 are isolated and treated according to the first three steps of the method outlined above, namely:

a. obtaining, from a subject, a biological sample having subject genomic DNA;

b. extracting or otherwise isolating the genomic DNA;

c. treating the genomic DNA of b), or a fragment thereof, with one or more reagents to convert cytosine bases that are unmethylated in the 5-position thereof to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties;

and wherein the subsequent amplification of d) is carried out in a methylation specific manner, namely by use of methylation specific primers or *blocking oligonucleotides*, and further wherein the detection of the amplificates is carried out by means of a real-time detection probes, as described above.

Wherein the subsequent amplification of d) is carried out by means of methylation specific primers, as described above, said methylation specific primers comprise a sequence having a length of at least 9 nucleotides which hybridizes to a pretreated nucleic acid sequence according to one of SEQ ID NO: 60 to SEQ ID NO: 295 and sequences complementary thereto, wherein the base sequence of said oligomers comprises at least one CpG dinucleotide.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that said *blocking oligonucleotide* nucleotide sequence(s) hybridizes to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that said *blocking oligonucleotide* nucleotide sequence(s) hybridizes to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that said *blocking oligonucleotide* nucleotide sequence(s) hybridizes to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Step e) of the method, namely the detection of the specific amplificates indicative of the methylation status of one or more CpG positions according to SEQ ID NO: 1 to SEQ ID NO 59 is carried out by means of real-time detection methods as described above.

In an alternative most preferred embodiment of the method the subsequent amplification of d) is carried out in the presence of *blocking oligonucleotides*, as described above. Said *blocking oligonucleotides* comprising a sequence having a length of at least 9 nucleotides which hybridizes to a pretreated nucleic acid sequence according to one of SEQ ID NO: 60 to SEQ ID NO: 295 and sequences complementary thereto, wherein the base sequence of said oligomers comprises at least one CpG, TpG or CpA dinucleotide. Step e) of the method, namely the detection of the specific amplificates indicative of the methylation status of one or more CpG positions according to SEQ ID NO: 1 to SEQ ID NO 59 is carried out by means of real-time detection methods as described above.

In a further preferred embodiment of the method the nucleic acids according to SEQ ID NO: 1 to SEQ ID NO 58 are isolated and treated according to the first three steps of the method outlined above, namely:

a) obtaining, from a subject, a biological sample having subject genomic DNA;

b) extracting or otherwise isolating the genomic DNA;

c) treating the genomic DNA of b), or a fragment thereof, with one or more reagents to convert cytosine bases that are unmethylated in the 5-position thereof to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties; and wherein

d)amplifying subsequent to treatment in c) is carried out in a methylation specific manner, namely by use of methylation specific primers or *blocking oligonucleotides*, and further wherein

e)detecting of the amplificates is carried out by means of a real-time detection probes, as described above.

Wherein the subsequent amplification of c) is carried out by means of methylation specific primers, as described above, said methylation specific primers comprise a sequence having a length of at least 9 nucleotides which hybridizes to a pretreated nucleic acid sequence according to one of SEQ ID NO: 60 to SEQ ID NO: 295 and sequences complementary thereto, wherein the base sequence of said oligomers comprises at least one CpG dinucleotide.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that said methylation specific primers

hybridize to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that said methylation specific primers hybridize to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that said methylation specific primers hybridize to a pretreated nucleic acid sequence according to one of the pretetreated sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Additional embodiments of the invention provide a method for the analysis of the methylation status of genomic DNA according to the invention (SEQ ID NO: 1 to SEQ ID NO: 59 , and complements thererof) without the need for pretreatment.

Wherein the method is for the differentiation of one of normal prostate and/or BPH from prostate cancer it is particularly preferred that the analysis is carried out on genomic sequences according to Table 4, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of one of normal prostate, normal tissue from other tissues, cancer of other tissues and/or BPH from prostate cancer it is particularly preferred that the analysis is carried out on genomic sequences according to Table 5, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

Wherein the method is for the differentiation of prostate cancer from cancers of other tissues it is particularly preferred that the analysis is carried out on genomic sequences according to Table 6, said contiguous nucleotides comprising at least one CpG, TpG or CpA dinucleotide sequence.

In the *first step* of such additional embodiments, the genomic DNA sample is isolated from tissue or cellular sources. Preferably, such sources include cell lines, histological slides, body fluids, or tissue embedded in paraffin. In the *second step*, the genomic DNA is extracted. Extraction may be by means that are standard to one skilled in the art, including but not limited to the use of detergent lysates, sonification and vortexing with glass beads. Once

the nucleic acids have been extracted, the genomic double-stranded DNA is used in the analysis.

In a preferred embodiment, the DNA may be cleaved prior to the treatment, and this may be by any means standard in the state of the art, in particular with methylation-sensitive restriction endonucleases.

In the *third step*, the DNA is then digested with one or more methylation sensitive restriction enzymes. The digestion is carried out such that hydrolysis of the DNA at the restriction site is informative of the methylation status of a specific CpG dinucleotide.

In the *fourth step*, which is optional but a preferred embodiment, the restriction fragments are amplified. This is preferably carried out using a polymerase chain reaction, and said amplificates may carry suitable detectable labels as discussed above, namely fluorophore labels, radionucleotides and mass labels.

In the *fifth step* the amplificates are detected. The detection may be by any means standard in the art, for example, but not limited to, gel electrophoresis analysis, hybridization analysis, incorporation of detectable tags within the PCR products, DNA array analysis, MALDI or ESI analysis.

In the final step the of the method the presence, absence or subclass of prostate cell proliferative disorder is deduced based upon the methylation state of at least one CpG dinucleotide sequence of SEQ ID NO 1 to SEQ ID NO 59, or an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotide sequences of SEQ ID NO 1 to SEQ ID NO 59.

Diagnostic assays for prostate cell proliferative disorders

The present invention enables diagnosis of events which are disadvantageous to patients or individuals in which important genetic and/or epigenetic parameters within one or more of SEQ ID NO: 1 to SEQ ID NO: 59 may be used as markers. Said parameters obtained by means of the present invention may be compared to another set of genetic and/or epigenetic parameters, the differences serving as the basis for a diagnosis of events which are disadvantageous to patients or individuals.

Specifically, the present invention provides for diagnostic cancer assays based on measurement of differential methylation of one or more CpG dinucleotide sequences of SEQ ID NO: 1 to SEQ ID NO: 59 , or of subregions thereof that comprise such a CpG dinucleotide sequence. Typically, such assays involve obtaining a tissue sample from a test tissue, performing an assay to measure the methylation status of at least one of one or more CpG

dinucleotide sequences of SEQ ID NO: 1 to SEQ ID NO: 59 derived from the tissue sample, relative to a control sample, or a known standard and making a diagnosis or prognosis based thereon.

In particular preferred embodiments, inventive oligomers are used to assess the CpG dinucleotide methylation status, such as those based on SEQ ID NO: 1 to SEQ ID NO: 295, or arrays thereof, as well as in kits based thereon and useful for the diagnosis of prostate cell proliferative disorders.

Kits

Moreover, an additional aspect of the present invention is a kit comprising, for example: a bisulfite-containing reagent; a set of primer oligonucleotides containing at least two oligonucleotides whose sequences in each case correspond, are complementary, or hybridize under stringent or highly stringent conditions to a 16-base long segment of the sequences SEQ ID NO: 1 to SEQ ID NO: 295; oligonucleotides and/or PNA-oligomers; as well as instructions for carrying out and evaluating the described method. In a further preferred embodiment, said kit may further comprise standard reagents for performing a CpG position-specific methylation analysis, wherein said analysis comprises one or more of the following techniques: MS-SNuPE, MSP, MethyLight ™, HeavyMethyl™, COBRA, and nucleic acid sequencing. However, a kit along the lines of the present invention can also contain only part of the aforementioned components.

While the present invention has been described with specificity in accordance with certain of its preferred embodiments, the following example serves only to illustrate the invention and is not intended to limit the invention within the principles and scope of the broadest interpretations and equivalent configurations thereof.

EXAMPLES

In the following 'uL' is taken to mean 'microlitre' i.e. 10^{-6} litres, accordingly 'uM' is taken to mean 'micromolar'.

Pooled genomic DNA was isolated and analyzed using the discovery methods, AP-PCR and MCA (Example 1). These technologies distinguish between methylated and unmethylated CpG sites through the use of methylation sensitive enzymes. In general, whole genomic DNA is first digested to increase manageability, and then further digested with a methylation sensitive restriction enzyme. Methylated fragments are preferentially amplified because cleavage at the unmethylated sites prevents amplification of these products. Differentially methylated fragments identified using these techniques are sequenced (Example 2) and compared to the human genome using the BLAST utility in the Ensembl database. The sample set was selected based on the initial aim of the diagnostic problem to be solved, namely the improved detection and discrimination of prostate carcinomas from normal or benign conditions. The following comparisons were run using three "All Cancer" prostate cancer sample pools (10,10, and 20 samples each), two benign prostate hyperplasia (BPH) sample pools (10 samples each), three low grade prostate cancer sample pools (10 samples each), three high grade prostate cancer sample pools (10 samples each), and one peripheral blood lymphocytes (PBL) pool (9 samples)]:

- BPH vs. All Cancer (High & low Gleason score; transitional (TZ) and peripheral (PZ) zones, 2 comparisons)
- BPH vs. Low Gleason Score (Gleason < 6, TZ & PZ represented, 2 comparisons)
- BPH vs. High Gleason Score (Gleason > 7, TZ & PZ represented, 2 comparisons)
- Low Gleason Score vs. High Gleason Score (for MCA, each pool was used as tester and driver)
- BPH vs. PBLs
- All cancer vs. PBLs

The BPH vs. PBLs comparison was not done for APPCR.

For all MCA comparisons that included cancer samples, the cancer was the tester. The low to high Gleason score comparison was run twice, once with low as the tester, and once with high

as the tester, bringing the total number of comparisons for MCA to ten. In the experiments with PBLs, the PBL sample was the driver. See Table 1.

Table 1: Sample pools used in comparison studies (AP-PCR and MCA)

Comparison	Nickname	Pool Type	Pool #	Samples per pool	Sample Breakdown			
					Gleas < 6 / Trans. Zone	Gleas < 6 / Periph Zone	Gleas >7 Trans. Zone	Gleas >7 Periph Zone
BPH vs. All cancers	BA1	BPH	1	10	10 BPH			
		All	1	10	2	3	2	3
BPH vs. All cancers	BA2	BPH	2	10	5 BPH, 5 Normal			
		All	2	10	3	2	3	2
BPH vs. Low	BL1	BPH	1	10	10 BPH			
		Low	1	10	5	5	0	0
BPH vs. Low	BL2	BPH	2	10	5 BPH, 5 Normal			
		Low	2	10	5	5	0	0
BPH vs. High	BH1	BPH	1	10	10 BPH			
		High	1	10	0	0	5	5
BPH vs. High	BH2	BPH	2	10	5 BPH, 5 Normal			
		High	2	10	0	0	5	5
Low vs. High	HL	Low	3	10	5	5	0	0
		High	3	10	0	0	5	5
BPH vs. PBLs	BP	BPH	1	10	10 BPH			
		PBL	1	9	9 PBL's			
Cancer vs. PBL	CP	All	3	20	5	5	5	5
		PBL	1	9	9 PBL's			

Example 1: MCA and AP-PCR

Identifying one or more *primary* differentially methylated CpG dinucleotide sequences using a controlled assay suitable for identifying at least one differentially methylated CpG dinucleotide sequence within the entire genome, or a representative fraction thereof.

All processes were performed on both pooled and/or individual samples, and analysis was carried out using two different Discovery methods; namely, methylated CpG amplification (MCA), and arbitrarily-primed PCR (AP-PCR).

AP-PCR. AP-PCR analysis was performed on sample classes of genomic DNA as follows:

1. DNA isolation; genomic DNA was isolated from sample classes using the commercially available Wizard™ kit;

2. Restriction enzyme digestion; each DNA sample pool was digested with 3 different sets of restriction enzymes for 16 hours at 37°C: RsaI (recognition site: GTAC); RsaI (recognition site: GTAC) plus HpaII (recognition site: CCGG; sensitive to methylation); and RsaI (recognition site: GTAC) plus MspI (recognition site: CCGG; insensitive to methylation);

3. AP-PCR analysis; each of the restriction digested DNA samples was amplified with the primers listed in TABLE 2 at a 40°C annealing temperature, and with ^{33}P dATP in the primer sets outlined in Table 3.

4. Polyacrylamide Gel Electrophoresis; 1.6 μl of each AP-PCR sample was loaded on a 5% Polyacrylamide sequencing-size gel, and electrophoresed for 4 hours at 130 Watts. Gels were transferred to chromatography paper, covered with saran wrap, and dried in a gel dryer for a period of about 1-hour.

5. Autoradiographic Film Exposure; film was exposed to dried gels for 20 hours at minus 80°C, and then developed. Glogos II Autorad markers (Stratagene) were added to the dried gel and exposure was repeated with new film. The first autorad was retained for records, while the second was used for excising bands; and

6. Bands corresponding to differential methylation were visually identified on the gel. Such bands were excised and the DNA therein was isolated and cloned using the Invitrogen TA Cloning Kit.

Table 2: Primers used according to the AP-PCR Protocol Example 1

Name	SEQ ID NO:	Sequence
GC1	928	GGGCCGCGGC
GC2	929	CCCCGCGGGG
GC3	930	CGCGGGGGCG
GC4	931	GCGCGCCGCG
GC5	932	GCGGGGCGGC
G1	933	GCGCCGACGT
G2	934	CGGGACGCGA
G3	935	CCGCGATCGC
G4	936	TGGCCGCCGA
G5	937	TGCGACGCCG
G6	938	ATCCCGCCCG
G7	939	GCGCATGCGG
G8	940	GCGACGTGCG
G9	941	GCCGCGNGNG
G10	942	GCCCGCGNNG
APBS1	943	AGCGGCCGCG

APBS5	944	CTCCCACGCG
APBS7	945	GAGGTGCGCG
APBS10	946	AGGGGACGCG
APBS11	947	GAGAGGCGCG
APBS12	948	GCCCCCGCGA
APBS13	949	CGGGGCGCGA
APBS17	950	GGGGACGCGA
APBS18	951	ACCCCACCCG

Table 3

Combination	primer 1	primer 2	primer 3
101	GC1	G2	APBS1
103	GC3	G4	APBS1
105	GC5	G6	APBS1
107	GC2	G8	APBS5
109	GC4	G10	APBS5
111	GC1	G8	APBS7
113	GC3	G6	APBS7
115	GC5	G4	APBS7
117	GC2	G2	APBS10
119	GC4	G2	APBS10
121	GC1	G4	APBS11
123	GC3	G5	APBS11
125	GC5	G7	APBS11
127	GC2	G9	APBS12
129	GC4	G9	APBS12
131	GC1	G7	APBS13
133	GC3	G5	APBS13
135	GC5	G3	APBS13
137	GC2	G1	APBS17
139	GC4	G3	APBS17
141	GC1	G5	APBS18
143	GC3	G7	APBS18
145	GC5	G9	APBS18
147	G2	G3	APBS17
149	G4	G5	APBS17
151	G6	G7	APBS17
153	G8	G9	APBS13
155	G8	G10	APBS13
157	G6	G8	APBS12
159	G4	G6	APBS12

161	G2	G4	APBS12
163	G2	G10	APBS11
165	G2	G5	APBS11
167	G4	G7	APBS10
169	G6	G9	APBS10
171	G1	G8	APBS10
173	G6	G10	APBS7
175	G4	G8	APBS7
177	G2	G6	APBS5
179	G4	G10	APBS5
181	G2	G8	APBS5
183	APBS1	APBS10	APBS11
185	APBS5	APBS7	APBS17
187	APBS1	APBS12	APBS18
189	APBS10	APBS13	APBS17
191	APBS5	APBS11	APBS12
193	APBS7	APBS10	APBS13
195	APBS1	APBS5	APBS11
197	APBS7	APBS17	APBS18
199	APBS1	APBS12	APBS13

MCA. MCA was used to identify hypermethylated sequences in one population of genomic DNA as compared to a second population by selectively eliminating sequences that do not contain the hypermethylated regions. This was accomplished, as described in detail herein above, by digestion of genomic DNA with a methylation-sensitive enzyme that cleaves un-methylated restriction sites to leave blunt ends, followed by cleavage with an isoschizomer that is methylation insensitive and leaves sticky ends. This is followed by ligation of adaptors, amplicon generation and subtractive hybridization of the tester population with the driver population.

The initial restriction digestion reaction solutions contained the following:

DRIVERS:

DNA	510 uL
buffer 4	60 uL
100x BSA	6 uL
SmaI (20U/uL)	24 uL

TESTERS:

DNA	68 uL
buffer 4	10 uL
10x BSA	10 uL
SmaI (20U/uL)	2 uL

The reaction mixtures were incubated overnight at room temperature.
The pools were then further digested with Xma I (2 uL=100 U), 6 hours at 37°C. 2 uL (20U) XmaI was added to each tester digest and 8 uL (80U) to each driver digest

The cleaned-up, digested material was ligated to the adapter-primer RXMA24 + RXMA12 (Sequence: RXMA24: AGCACTCTCCAGCCTCTCACCGAC (SEQ ID NO: 952); RXMA12: CCGGGTCGGTGA (SEQ ID NO:953). These were hybridized to create the adapter by heating together at 70°C and slowly cooling to room temperature (RT) in a 30 uL reaction:

Each DNA	33 uL
T4 Buffer	6 uL
RXMA adapter-primer (100 uM)	20 uL
Ligase	1 uL

The reaction solution was incubated overnight at room temperature.
3 uL of the ligation mix for both tester and driver populations was used in each initial PCR to generate the starting amplicons. The reaction solutions were as follows:

TESTERS

100uM RXMA24	1 uL
PCR buffer	10 uL
25 mM dNTPs	1.2 uL
ddH20	68.8 uL
Titanium Taq	1 uL
100% DMSO	2 uL
5M Betaine	10 uL

3 uL ligated tester DNA was added to each 97 uL tester cocktail.

DRIVERS

Drivers are amplified with dUTP in place of dTTP:

100uM RXMA24	1 uL
PCR buffer	10 uL
25 mM dNTPs	1.2 uL
(25 mM each dATP, dCTP, dGTP, and dUTP)	
ddH20	68.8 uL
Titanium Taq	1 uL
100% DMSO	2 uL
5M Betaine	10 uL

3 uL ligated driver DNA was added to each 97 uL driver cocktail.

PCR conditions:

72 degrees 5 min

30 cycles:

95 degrees 1 min

72 degrees 3 min

Final extension:

72 degrees 10 min.

The tester amplicons were then digested with XmaI, yielding overhanging ends, and the driver amplicons were digested with SmaI, yielding blunt end fragments.

DRIVERS (SmaI):

DNA	500 uL
Buffer 4	100 uL
100x BSA	10 uL
H20	340 uL
SmaI (20U/uL)	50 uL

Total vol: 1 mL. Incubated overnight at room temp.

TESTERS (XmaI):

DNA	20 uL
buffer 4	10 uL
10x BSA	10 uL
H20	59 uL
XmaI (50U/uL)	1 uL

Total vol: 100 uL. Incubated overnight at 37 degrees.

A new set of adapter primers (hybridized as described for the above RXMA primers) JXMA24 + JXMA12 (Sequence: JXMA24: ACCGACGTCGACTATCCATGAACC (SEQ ID NO:954); JXMA12: CCGGGGTTCATG (SEQ ID NO:955) was ligated to the Tester in a Thermocycler at 16°C for 2 hours in the following reaction solution:

DNA	16 uL
T4 buffer	3 uL
JXMA-P adapter (100uM)	10 uL
T4 Ligase (400U/uL)	1 uL

The digested tester and driver amplicons were hybridized together. A selective PCR reaction was done using primer JXMA24 (SEQ ID NO:954). The reaction solution contained:

JXMA24	0.5 uL
taq buffer	5 uL
dNTPs	0.6 uL
ddH20	27.4 uL
betaine	5 uL
DMSO	1 uL
Titanium taq	0.5 uL
DNA	10 uL

PCR conditions:

72 degrees 8 min (fill in ends)

5 cycles:

95 degrees 1 min

72 degrees 3 min

final extension:
72 degrees 10 min

Subsequently, 20 uL of Mung Bean nuclease buffer plus 10 uL Mung Bean Nuclease (10U) was added and incubated at 37°C for 30 minutes. This reaction was cleaned up and used as a template for 25 more cycles of PCR using JXMA24 primer in the following reaction solution:

JXMA24	1 uL
taq buffer	10 uL
dNTPs	1.2 uL
ddH20	27 uL
betaine	10 uL
DMSO	2 uL
Titanium taq	1 uL
DNA	48 uL

under the following conditions.

95 degrees 2 min
30 cycles:
95 degrees 1 min
72 degrees 3 min
Final extension:
72 degrees 10 min
Hold at 4 degrees

The resulting PCR product (tester) was digested again using XmaI:
45 uL DNA
15 uL Buffer 4
15 uL 10x BSA
71 uL H20
4 uL XmaI

Incubated overnight at 37 degrees

A third adapter, NXMA24 (AGGCAACTGTGCTATCCGAGTGAC; SEQ ID NO:956) + NXMA12 (CCGGGTCACTCG; SEQ ID NO: 957) was ligated. The tester (500 ng) was hybridized a second time to the original digested driver (40 ug) in 4 uL EE (30 mM EPPS, 3 mM EDTA) and 1 uL 5 M NaCl at 67°C for 20 hours. Selective PCR was performed using NXMA24 primer as follows:

NXMA24	0.5 uL
taq buffer	5 uL
dNTPs	0.6 uL
ddH20	27.4 uL
betaine	5 uL
DMSO	1 uL
Titanium taq	0.5 uL
DNA	10 uL

PCR program:
72 degrees 8 min (fill in ends)
8 cycles:
95 degrees 1 min
72 degrees 3 min
final extension:
72 degrees 10 min
The reaction solution was held at 4 degrees

Subsequently, 20 uL of Mung Bean nuclease buffer plus 10 uL Mung Bean Nuclease (10U) was added and incubated at 30°C for 30 minutes. This reaction was cleaned up and used as a template for 25 more cycles of PCR using NXMA24 primer as follows:

Reaction solution

NXMA24	1 uL
taq buffer	10 uL
dNTPs	1.2 uL

ddH20	27 uL
betaine	10 uL
DMSO	2 uL
Titanium taq	1 uL
DNA	48 uL

PCR program:
95 degrees 2 min
30 cycles:
95 degrees 1 min
72 degrees 3 min
Final extension:
72 degrees 10 min
Hold at 4 degrees

The resulting PCR product was digested with XmaI :
Reaction solution:

DNA	38 uL
buffer 4	5 uL
10x BSA	5 uL
Xma I	2 uL

Incubated overnight at 37 degrees.

The DNA digest was then ligated into the vector pBC Sk—predigested with XmaI and phosphatased (675 ng). 5 uL of the ligation mixture was used to transform chemically competent TOP10™ cells according to the manufacturer's instructions. The transformations were plated onto LB/XGal/IPTG/CAM plates. Selected insert colonies were sequenced according to Example 2.

Example 1 resulted in a large number of unique sequences that were potential candidates for assay markers. A subset of these sequences was eliminated due their high (>50%) repeat content. A total of 480 unique sequences were identified in the comparisons performed for this study. A subset of these sequences were further selected using the following scoring procedure:

- Appearance using multiple methods
- Appearance in multiple pools
- Located within CpG island
- Located within the promoter region of a gene
- Near or within predicted or known gene
- Known to be associated with disease
- Class of gene (transcription factor, growth factor, etc.)
- Repetitive element (negative score)

Under this scoring scheme, a MeST sequence receives a point for each of the above criteria, and receives a score of (-)8 for having repetitive sequence content greater than 50%. The highest score possible is 7, the lowest is (-)8. Scores are automatically generated using a proprietary database. Of the initial set of 480 MeST sequences, 277 scored 0 or higher. Using the scoring criteria above, along with manual review of the sequences, the number of candidate MeST was further reduced to 126 unique sequences.

Primer design for the 126 sequences was then initiated for the purpose of bisulfite sequencing. Thirty five of the sequences were discarded for various reasons including inability to design adequate primers, failure of amplification from control DNA, or if further scrutiny of the sequence or updates of the Ensembl database revealed poor quality or repeat sequences not previously noted.

Example 2: Bisulfite Sequencing

For bisulfite sequencing amplification primers were designed to cover each identified MeST sequence when possible or part of the 1000 bp upstream or 1000 bp downstream flanking regions surrounding the position. Samples used in Example 1 were utilized for amplicon production in this phase of the study. Each sample was treated with sodium bisulfite and sequenced. Sequence data was obtained using ABI 3700 sequencing technology. Obtained

sequence traces were normalized and percentage methylation calculated using Epigenomic's proprietary ESME bisulphite sequence sequencing trace analysis program.

Results of bisulfite sequencing

The following properties were noted:

1. Bisulfite sequencing indicates differential methylation of a CpG site between selected classes of samples (fisher score)
2. Co-methylation is observed
3. If only one site has Fisher score >1, are there additional sites surrounding with fisher score > 0.5?
4. Are there trends in the pattern?-blocks of blue vs yellow (not necessarily high fisher score)

Genomic regions that were considered to demonstrate significant co-methylation as assesed by these criteria then proceeded to further investigation.

Figures 1 to 3 are ranked matrices produced from bisulfite sequencing data analysed by the Epigenomics' proprietary 'ESME' program. The overall matrix represents the sequencing data for one region of interest. Each row of the matrix is a single CpG site within the fragment and each column is an individual DNA sample. The bar on the left represents a scale of the percent methylation, with the degree of methylation represented by the shade of each position within the column from black representing 100% methylation to light grey representing 0% methylation. No data was available for white positions.

Figure 1 shows the sequencing data of a fragment of the gene Prostaglandin E2 Receptor, EP4 Subtype. Here, bisulfite sequencing showed differential but non-conclusive patterns of methylation between samples. The gene was further investigated on a larger sample set using the array process (Example 3) as the accuracy of this gene as a marker could be improved when analysed in combination with other genes.

Figure 2 shows the sequencing data of a fragment of the gene Orphan Nuclear Receptor (a-1Fetoprotein Transcription Factor). In this case, bisulfite sequencing indicated differential methylation or comethylation between sample types.

Figure 3 shows the sequencing data of a fragment of the gene 1-Acyl-SN-Glycerol-3-Phosphate Acyltransferase Gamma. This was representative , of a subset of ROIs for which only poor quality sequence reads was obtained and the gene was only able to be meaningfully analysed using the array process (Example 3)

Example 3: Array analysis

A selection of the differentially methylated genomic regions were tehn further analysed by means of high throughput array analysis. The most useful final assay suitable for a diagnostic/classification screening test would enable analysis of body fluids such as serum, plasma or urine sediment (obviating the need for invasive procedures). Therefore, the sample set included DNA samples from other cancers which may be present in blood to provide more specific marker sets for sensitive assays.

Description of sample set for chip study

The sample set for the microarray analysis was designed to provide information concerning both the sensitivity and specificity of the marker candidates. A large number of samples (Table 7) from prostate cancer, BPH and normal prostate were screened. Prostate cancer samples were grouped by Gleason Score (High ($\geq$ 8), Moderate (7), and Low ($\leq$ 6)) and by zone (peripheral or transitional). The distribution of BPH samples was random, but because most BPH is derived from the transitional zone, it can be assumed that most samples were of that origin. In addition to prostate samples, a number of other cancer types were included to test for specificity to the prostate. The proposed samples for the study included the tissues in Table 7. PBL samples were included because of the proposed use of these markers in a blood based screen. Normal liver and liver cancer were also included because of the observed methylation of GSTP1 in these samples.

Sample Type	Sample Type
Prostate Cancers	Endocrine Related Cancers
• High Grade (Gleason $\geq$ 8)	• Breast
• Transitional Zone	• Male
• Peripheral Zone	• Female
• Low Grade (Gleason $\leq$ 6)	• Ovarian
• Transitional Zone	• Uterine
• Peripheral Zone	Other Cancers
• Moderate Grade (Gleason = 7)	• Liver
• Transitional Zone	• Lung
• Peripheral Zone	• Esophageal
• Additional Prostate Cancers	• Salivary Gland
• Post hormone therapy	• Stomach
Benign Prostate Disease	• Pancreatic
• BPH	• Melanoma
• Benign Fibroma	• Colon
• Prostatitis	Other Normal tissues
Genitourinary Tract Cancers	• Prostate
• Bladder	• Transitional
• Testicular	• Peripheral
• Kidney	• Additional
	• Bladder
	• Kidney
	• Liver
	• Testes
	• Sperm
	• Ureter
	• PBLs

Table 7. Overview of samples for the array study.

DNA extraction

Samples were received from either as frozen tissue or extracted genomic DNA. All DNA samples were extracted using Qiagen Genomic Tip-500 columns or the MagnaPure device.

Bisulfite treatment and multiplex PCR

Total genomic DNA of all samples was bisulfite treated to convert unmethylated cytosines to uracil. Methylated cytosines remained conserved as cytosines. Bisulfite treatment was performed using Epigenomics' proprietary bisulfite treatment process. Two independent bisulfite reactions were performed per patient sample. After bisulfitation 10 ng of each DNA sample was used in subsequent multiplex PCR (mPCR) reactions containing 7-8 primer pairs.

Hybridization

Each reaction contained the following:

0.4 mM each dNTPS

1 Unit Taq Polymerase

2.5 ul PCR buffer

3.5 mM MgCl2

80 nM Primerset (12-16 primers)

11.25 ng DNA (bisulfite treated)

Further details of the primers are shown in TABLE 8.

Forty cycles were carried out as follows: Denaturation at 95°C for 15 min, followed by annealing at 55°C for 45 sec., primer elongation at 65°C for 2 min. A final elongation at 65°C was carried out for 10 min.

Hybridization

All PCR products from each individual sample were then hybridised to glass slides carrying a pair of immobilised oligonucleotides for each CpG position under analysis. Each of these detection oligonucleotides was designed to hybridise to the bisulphite converted sequence around one CpG site which was either originally unmethylated (TG) or methylated (CG). See Table 2 for further details of all hybridisation oligonucleotides used (both informative and non-informative.) Hybridisation conditions were selected to allow the detection of the single nucleotide differences between the TG and CG variants.

5 ul volume of each multiplex PCR product was diluted in 10 x Ssarc buffer. The reaction mixture was then hybridised to the detection oligonucleotides as follows.

Denaturation at 95°C, cooling down to 10°C, hybridisation at 42°C overnight followed by washing with 10 x SSARC and dH_2O at 42°C.

Further details of the hybridisation oligonucleotides are shown in TABLE 9.

Fluorescent signals from each hybridised oligonucleotide were detected using genepix scanner and software. Ratios for the two signals (from the CG oligonucleotide and the TG oligonucleotide used to analyse each CpG position) were calculated based on comparison of intensity of the fluorescent signals.

For each patient, 2 DNA aliquots were bisulfite treated and for each bisulfite treated DNA sample two hybridizations were performed, resulting in a total of 4 chips processed per patient. For hybridization, the samples were grouped into 2 processing rounds in order to avoid a potential process-bias. As stated, each of the 2 rounds included a 2 fold redundancy for each DNA sample for the 4-fold redundancy per patient. The samples were hybridized in batches of 112 samples randomized for sex, diagnosis, tissue, and bisulfite batch .

Data analysis methods

Analysis of the chip data

For the analysis of the chip data Epigenomics' proprietary software "EpiScape" was used. It encompasses a variety of statistical tools and novel machine learning methods for analyzing and visualizing methylation array data. In the following sections we summarize the most important data analysis techniques that we applied for analyzing the data.

From raw hybridization intensities to methylation ratios

- The log methylation ratio (log(CG/TG)) at each CpG position is determined according to a standardized preprocessing pipeline. This log ratio has the property that the hybridization noise has approximately constant variance over the full range of possible methylation rates.

Hypothesis testing

Our main task was to identify markers that can make a significant contribution to the class prediction of samples. For the 'particularly prefered embodiments' of the invention the significant contribution is detected when the null-hypothesis that a prediction model including the marker does not improve classification performance over a model without the marker can be rejected with $p<0.05$. Because we apply this test to a whole set of potential markers, we corrected the p-values for multiple testing. We did this by applying the conservative

Bonferroni correction, which simply multiplies the single marker p-values with the number of potential markers tested. We also give results with the less conservative False Discovery Rate (FDR) method.

Throughout this example a marker (sometimes also simply referred to as gene or amplicon) is also referred to as a genomic region of interest (ROI). It comprises of several CpG positions in the respective genomic region. For testing the null hypothesis that a marker has no predictive power we use the likelihood ratio test for logistic regression models. The logistic regression model for a single marker is a linear combination of methylation measurements from all CpG positions in the respective ROI. The fitted logistic regression model is compared to a constant probability model that is independent of methylation and represents the null hypothesis. The p-value of the marker is computed via the likelihood ratio test.

A significant p-value for a marker means that the methylation of this ROI has some systematic correlation to the question of interest as given by the two classes. In general a significant p-value does not necessarily imply a good classification performance. However, because with logistic regression we use a linear predictor as the basis of our test statistic small p-values will be indicative of a good clinical performance.

Class prediction by supervised learning

In order to give a reliable estimate of how well the CpG ensemble of a selected marker can differentiate between different tissue classes we can determine its prediction accuracy by classification. For that purpose we calculated a methylation profile-based prediction function using a certain set of tissue samples with a specific class label. This step is called training and it exploits the prior knowledge represented by the data labels. The prediction accuracy of that function is then tested on a set of independent samples. As a method of choice, we use the support vector machine (SVM) algorithm to learn the prediction function. In this analysis, sensitivity and specificity were weighted equally. This is achieved by setting the risk associated with false positive and false negative classifications to be inversely proportional to the respective class sizes. Therefore sensitivity and specificity of the resulting classifier can be expected to be approximately equal. Note that this weighting can be adapted according to the clinical requirements.

Estimating the performance of the tissue class prediction: Cross Validation

With limited sample size the cross-validation method provides an effective and reliable estimate for the prediction accuracy of a discriminator function, and therefore in addition to

the significance of the markers we provide cross-validation accuracy, sensitivity and specificity estimates. For each classification task, the samples were partitioned into 5 groups of approximately equal size. Then the learning algorithm was trained on 4 of these 5 sample groups. The predictor obtained by this method was then tested on the remaining group of independent test samples. The number of correct positive and negative classifications was counted over 10 runs for the learning algorithm for all possible choices of the independent test group without using any knowledge obtained from the previous runs. This procedure was repeated on 10 random permutations of the sample set giving a better estimate of the prediction performance than if performed by simply splitting the samples into one training sample set and one independent test set.

Data analysis results

Our first step in analysis of the array data was to look at discriminatory markers in a comparison of all tissues of prostatic origin. We first compared normal and BPH prostate tissue against prostate cancer samples, and found that many of the markers used in this study have p-values meeting the desired criteria (Figure 4). Next, we compared prostate cancer tissues to all other tissue classes used in this study (Table 7). Almost all markers met the specified statistical criteria with this sample set. The GSTP1 gene is known to be hypermethylated in prostate cancer, but also displays hypermethylation in other cancers. Therefore, our final comparison was a more detailed examination of the methylation levels in prostate cancer versus other cancer types.

Prostate Normal and BPH vs. Prostate Cancer

In this comparison, the negative class consists of 91 samples from normal prostate, and BPH. The positive class consists of 99 prostate cancer samples. Most of the markers meet the criteria of p-value < 0.05 (Figure 4). The p-values, accuracy, sensitivity and specificity of the analysis are shown in Table 4. The best 12 markers are further shown in Figure 5.

Prostate Normal and Other Tissues vs. Prostate Cancer

Comparisons were then performed on the complete sample set. The negative group was expanded to include normal tissue from other organs and cancer of other origins than prostate,

according to table 7. The negative class consists of 254 samples from normal prostate, BPH and other normal and cancerous tissues. The positive class consists of 99 prostate cancer samples. Again the p-values for most markers meet the significance level of p= < 0.05 (Table 5). The accuracy of the highest performing marker is ~ 86% (see figure 6 and/or table 5). The p-values, accuracy, sensitivity and specificity of the analysis are shown in Table 5. The best 12 markers are further shown in Figure 7.

Other Cancers vs. Prostate Cancer

Since hypermethylation of GSTP1 (state of the art methylation prostate cancer marker) is not specific to the prostate, we examined the methylation status of prostate cancer and other cancers in greater detail. Figure 16 shows that GSTP1 (SEQ ID NO:57) was strongly hypermethylated in liver cancer and to a lesser degree in breast cancer. Nevertheless, several other of the best candidate markers distinguish well between cancer of the prostate and liver. The p-values, accuracy, sensitivity and specificity of the analysis are shown in Table 5. The best 12 markers are further shown in Figure 8.

Tables 4-6 below summarize the performance characteristics of all markers in the following comparisons:

Normal Prostate and BPH vs. Prostate Cancer (Table 4)

Normal Prostate, BPH and other tissues vs. Prostate Cancer (Table 5)

Other Tissues vs. Prostate Cancer (Table 6)

The analyses in tables 4 and 5 contained BPH and normal prostate samples in the analysis group. The analysis for Normal Prostate and BPH vs. Prostate Cancer was designed to determine the performance of the markers in a prostate specific environment. The analysis that included other tissues, both cancer and normals (Normal Prostate, BPH and Other Tissues vs. Prostate Cancer) took into consideration the performance of the markers with a background that may contribute or alter the overall performance of the markers in remote samples.

Cancer types (table 6) were also compared because of the propensity for GSTP1 to be methylated in multiple cancer types. This type of lack of specificity could have a negative impact on the performance of a marker in body fluid-based assays. GSTP1 (SEQ ID NO: 57) is highly methylated in prostate cancer, but also in liver cancer as anticipated. IGF2 (SEQ ID NO: 58) is similarly methylated in liver cancer. The majority of the markers shown in Figure 8 are unmethylated in most cancer types, with the exception of prostate cancer. From Figures 4-8, it can be observed that there are multiple candidates that have the potential to be informative and accurate

markers. It is recommended that multiple markers be combined to ensure a high sensitivity and specificity.

Table 4: **Normal Prostate, BPH and Other Tissues vs. Prostate Cancer**

Genomic SEQ ID NO:	Treated Methylated sense strand SEQ ID NO:	Treated Methylated Antisense strand SEQ ID NO:	Treated Unmethylated SEQ ID NO:	Treated Unmethylated antisense sense strand strand SEQ ID NO:	P-value	Accuracy	Sensitivity	Specificity
57	172	173	290	291	1.30E-027	0.86	0.67	0.93
23	104	105	222	223	2.00E-029	0.81	0.75	0.83
36	130	131	248	249	3.80E-018	0.75	0.75	0.76
56	170	171	288	289	1.10E-012	0.74	0.62	0.79
11	80	81	198	199	5.10E-019	0.74	0.76	0.74
20	98	99	216	217	4.90E-016	0.73	0.77	0.71
22	102	103	220	221	1.10E-009	0.7	0.61	0.74
31	120	121	238	239	6.90E-018	0.7	0.79	0.66
30	118	119	236	237	1.60E-012	0.69	0.81	0.64
58	174	175	292	293	1.20E-011	0.68	0.71	0.67
34	126	127	244	245	5.50E-009	0.68	0.65	0.69
41	140	141	258	259	1.50E-008	0.67	0.7	0.66
59	176	177	294	295	4.90E-007	0.67	0.59	0.7
51	160	161	278	279	1.50E-012	0.67	0.76	0.63
24	106	107	224	225	1.30E-006	0.67	0.67	0.67
18	94	95	212	213	1.10E-014	0.67	0.84	0.6
54	166	167	284	285	3.80E-007	0.66	0.7	0.65
27	112	113	230	231	6.60E-007	0.66	0.7	0.64
7	72	73	190	191	8.30E-005	0.65	0.62	0.67
35	128	129	246	247	1.00E-004	0.65	0.53	0.69
16	90	91	208	209	7.50E-011	0.64	0.77	0.6
38	134	135	252	253	1.20E-004	0.64	0.63	0.64
14	86	87	204	205	5.20E-008	0.63	0.72	0.6
25	108	109	226	227	3.50E-011	0.62	0.79	0.56
1	60	61	178	179	8.20E-005	0.62	0.67	0.6
28	114	115	232	233	1.40E-003	0.62	0.67	0.59
43	144	145	262	263	3.70E-002	0.61	0.56	0.63
4	66	67	184	185	4.40E-004	0.61	0.64	0.59
26	110	111	228	229	5.60E-003	0.6	0.64	0.59
12	82	83	200	201	3.00E-004	0.58	0.75	0.52
21	100	101	218	219	1.80E-002	0.57	0.64	0.54
33	124	125	242	243	1.10E-002	0.56	0.66	0.53

Table 5: Normal Prostate and BPH vs. Prostate Cancer

Genomic SEQ ID NO:	Treated methylated sense strand SEQ ID NO:	Treated methylated antisense strand SEQ ID NO:	Treated unmethylated sense strand SEQ ID NO:	Treated unmethylated antisense strand SEQ ID NO:	P-value	Acc	Sens	Specificity
57	172	173	290	291	4.60E-023	0.85	0.77	0.93
36	130	131	248	249	8.10E-019	0.81	0.75	0.86
23	104	105	222	223	6.10E-019	0.8	0.75	0.85
34	126	127	244	245	3.10E-015	0.78	0.71	0.86
20	98	99	216	217	1.60E-016	0.78	0.75	0.8
31	120	121	238	239	5.20E-015	0.76	0.71	0.81
59	176	177	294	295	1.90E-014	0.76	0.68	0.84
56	170	171	288	289	2.00E-013	0.76	0.65	0.53
30	118	119	236	237	5.90E-011	0.75	0.76	0.75
48	154	155	272	273	2.70E-011	0.74	0.71	0.78
54	166	167	284	285	1.20E-009	0.74	0.72	0.76
11	80	81	198	199	1.00E-010	0.74	0.69	0.8
24	106	107	224	225	1.10E-011	0.72	0.67	0.78
14	86	87	204	205	3.50E-009	0.71	0.63	0.8
18	94	95	212	213	3.10E-010	0.71	0.76	0.66
28	114	115	232	233	7.80E-008	0.71	0.69	0.72
8	74	75	192	193	4.10E-008	0.7	0.72	0.68
7	72	73	190	191	3.00E-004	0.7	0.62	0.78
4	66	67	184	185	6.30E-009	0.69	0.66	0.72
35	128	129	246	247	1.40E-008	0.69	0.59	0.8
27	112	113	230	231	1.40E-006	0.69	0.68	0.7
58	174	175	292	293	8.90E-006	0.68	0.65	0.71
26	110	111	228	229	1.20E-008	0.68	0.69	0.66
22	102	103	220	221	3.40E-008	0.67	0.57	0.78
41	140	141	258	259	7.90E-005	0.66	0.67	0.66
37	132	133	250	251	1.70E-006	0.66	0.6	0.73
1	60	61	178	179	7.40E-005	0.66	0.72	0.6
49	156	157	274	275	1.80E-005	0.66	0.62	0.71
16	90	91	208	209	1.30E-003	0.65	0.67	0.62
2	62	63	180	181	1.50E-002	0.64	0.66	0.63
44	146	147	264	265	7.50E-004	0.64	0.67	0.6
32	122	123	240	241	2.50E-003	0.64	0.59	0.69
13	84	85	202	203	5.10E-002	0.63	0.61	0.66
47	152	153	270	271	2.00E-002	0.63	0.64	0.61
42	142	143	260	261	3.30E-003	0.62	0.67	0.57
55	168	169	286	287	7.10E-003	0.62	0.67	0.57
29	116	117	234	235	5.10E-002	0.62	0.64	0.59
3	64	65	182	183	1.30E-001	0.61	0.59	0.64
50	158	159	276	277	1.00E+000	0.6	0.64	0.56
51	160	161	278	279	2.90E-002	0.6	0.65	0.56
43	144	145	262	263	9.60E-002	0.6	0.6	0.61
21	100	101	218	219	6.20E-001	0.59	0.66	0.52
46	150	151	268	269	3.00E-001	0.59	0.59	0.59
10	78	79	196	197	5.50E-001	0.59	0.52	0.66
38	134	135	252	253	5.10E-001	0.58	0.55	0.62
25	108	109	226	227	1.20E-002	0.57	0.52	0.63

15	88	89	206	207	1.00E+000	0.56	0.48	0.65
6	70	71	188	189	1.00E+000	0.56	0.63	0.48
33	124	125	242	243	1.00E+000	0.55	0.43	0.68
5	68	69	186	187	1.00E+000	0.55	0.6	0.5
9	76	77	194	195	1.00E+000	0.55	0.53	0.56
52	162	163	280	281	1.00E+000	0.54	0.48	0.6
40	138	139	256	257	1.00E+000	0.53	0.48	0.58
45	148	149	266	267	1.00E+000	0.52	0.38	0.68
17	92	93	210	211	1.00E+000	0.52	0.58	0.46
12	82	83	200	201	1.00E+000	0.47	0.36	0.58
39	136	137	254	255	1.00E+000	0.45	0.46	0.45
19	96	97	214	215	1.00E+000	0.4	0.46	0.32

Table 6: Other cancers vs. Prostate cancer

Genomic SEQ ID NO:	Treated methylated sense strand SEQ ID NO:	Treated methylated antisense strand SEQ ID NO:	Treated unmethylated sense strand SEQ ID NO:	Treated unmethylated antisense strand SEQ ID NO:	p-value	accuracy	sensitivity	specificity
57	172	173	290	291	9.7e-14	0.80	0.70	0.89
23	104	105	222	223	2.4e-19	0.78	0.75	0.81
25	108	109	226	227	6.9e-16	0.75	0.85	0.65
11	80	81	198	199	2.0e-13	0.75	0.76	0.73
51	160	161	278	279	2.0e-12	0.74	0.79	0.69
31	120	121	238	239	1.5e-13	0.74	0.92	0.58
16	90	91	208	209	1.1e-14	0.73	0.82	0.66
30	118	119	236	237	2.4e-08	0.73	0.82	0.64
10	78	79	196	197	5.5e-11	0.72	0.83	0.63
41	140	141	258	259	9.4e-07	0.70	0.73	0.66
18	94	95	212	213	5.0e-09	0.69	0.83	0.57
14	86	87	204	205	2.8e-09	0.69	0.86	0.55
20	98	99	216	217	9.2e-07	0.68	0.78	0.60
12	82	83	200	201	9.7e-07	0.68	0.76	0.61
36	130	131	248	249	6.1e-08	0.67	0.74	0.62
38	134	135	252	253	3.8e-05	0.67	0.66	0.69
22	102	103	220	221	4.1e-05	0.67	0.62	0.71
58	174	175	292	293	1.6e-08	0.66	0.73	0.61
46	150	151	268	269	6.6e-08	0.66	0.87	0.48
56	170	171	288	289	4.6e-05	0.66	0.60	0.72
27	112	113	230	231	1.4e-02	0.65	0.69	0.62
21	100	101	218	219	5.6e-05	0.64	0.70	0.59
15	88	89	206	207	4.5e-05	0.63	0.85	0.43
5	68	69	186	187	4.4e-06	0.63	0.73	0.54
42	142	143	260	261	2.8e-04	0.62	0.77	0.49
34	126	127	244	245	6.8e-03	0.62	0.70	0.55
7	72	73	190	191	3.0e-03	0.62	0.56	0.66
33	124	125	242	243	7.6e-02	0.61	0.72	0.52
28	114	115	232	233	7.2e-01	0.60	0.73	0.49
6	70	71	188	189	2.8e-01	0.60	0.65	0.55

1	60	61	178	179	9.5e-02	0.59	0.60	0.58
59	176	177	294	295	5.1e-02	0.59	0.62	0.56
43	144	145	262	263	4.2e-01	0.59	0.58	0.60
24	106	107	224	225	1.3e-01	0.59	0.76	0.43
37	132	133	250	251	1.1e-01	0.59	0.69	0.49
48	154	155	272	273	5.8e-01	0.59	0.72	0.47
4	66	67	184	185	4.2e-02	0.58	0.71	0.48
45	148	149	266	267	1.0e+00	0.58	0.79	0.40
39	136	137	254	255	3.1e-02	0.58	0.55	0.61
55	168	169	286	287	1.0e+00	0.58	0.69	0.48
26	110	111	228	229	7.3e-02	0.58	0.67	0.49
2	62	63	180	181	1.0e+00	0.57	0.63	0.52
54	166	167	284	285	8.2e-01	0.57	0.68	0.47
49	156	157	274	275	5.9e-02	0.56	0.82	0.34
8	74	75	192	193	1.0e+00	0.56	0.61	0.51
13	84	85	202	203	1.0e+00	0.56	0.59	0.53
32	122	123	240	241	1.0e+00	0.55	0.63	0.49
29	116	117	234	235	1.0e+00	0.55	0.55	0.55
19	96	97	214	215	1.0e+00	0.55	0.54	0.55
47	152	153	270	271	1.0e+00	0.54	0.84	0.29
9	76	77	194	195	9.7e-02	0.54	0.55	0.53
50	158	159	276	277	1.0e+00	0.54	0.62	0.47
52	162	163	280	281	1.0e+00	0.54	0.51	0.56
17	92	93	210	211	1.0e+00	0.54	0.49	0.57
44	146	147	264	265	1.0e+00	0.53	0.60	0.47
35	128	129	246	247	1.0e+00	0.52	0.45	0.59
3	64	65	182	183	1.0e+00	0.52	0.59	0.45
40	138	139	256	257	1.0e+00	0.51	0.56	0.47

TABLE 8

SEQ ID No:	*Primer:*	*Amplificate Length:*
(SEQ ID NO: 1)	TGGTATAGGAGGAGAAGAGTTG (SEQ ID NO: 296) TCAATCCCTAAAACCCAAA (SEQ ID NO: 297)	327
(SEQ ID NO: 2)	ACCCAAACTAACAATCAAAAAT (SEQ ID NO: 299) GGAAGGGAAGGATGAGAGTAT (SEQ ID NO: 298)	326
(SEQ ID NO: 3)	GGAAGGTTTAAGGTGAGAGAA (SEQ ID NO: 300) CAAAATAACCAATCCCCTAAA (SEQ ID NO: 301)	339
LIM/HOMEO BOX PROTEIN	CCCCAATATAAATCTACCAACC (SEQ ID NO: 303) TTATTTGAATTTTGGAGGTTATG	372

SEQ ID No:	*Primer:*	*Amplificate Length:*
LHX9 (SEQ ID NO: 4)	(SEQ ID NO: 302)	
(SEQ ID NO: 5)	TTAATGAAGTAGGGTTTGTATTGT (SEQ ID NO: 304) CCTCCAAAATCTTAACCAAAT (SEQ ID NO: 305)	421
(SEQ ID NO: 6)	CCCAACTAACTCAAATTCCAC (SEQ ID NO: 307) TTTATTTTAGGAGGGAAGGATT (SEQ ID NO: 306)	434
(SEQ ID NO: 7)	GTGGTTTTGGGGAATTAGTAT (SEQ ID NO: 308) CTCCTACATATCCCATCTCATC (SEQ ID NO: 309)	483
UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN) (SEQ ID NO: 8)	AATTAAGGTTTAGGGTTTTGTTT (SEQ ID NO: 310) ACCTTCCCTACAAATCTACCTAC (SEQ ID NO: 311)	365
BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN	ATAGTTTTGTGGGTTTAAGAGG (SEQ ID NO: 312) ACCCTAACCTTATACAATACCAAC (SEQ ID NO: 313)	414

SEQ ID No:	Primer:	Amplificate Length:
(SEQ ID NO: 9)		
BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	GGTGGGGTTATTAAGGAGTTTA (SEQ ID NO: 314) CTCAACTACCATACCCAAAAA (SEQ ID NO: 315)	480
(SEQ ID NO: 10)	TTGTGTTGGTTGTAAAAGGA (SEQ ID NO: 316) CAAACACTATACACCTCTCAACA (SEQ ID NO: 317)	428
(SEQ ID NO: 11)	TTGAGGTTATTGGTTTATAGATTTT (SEQ ID NO: 318) CCCTAACCACCCCTTCTA (SEQ ID NO: 319)	457
(SEQ ID NO: 12)	ACTCCATACACTTTTACCAACC (SEQ ID NO: 321) TGTGTGAAATGTTTTAGTTTAATTG (SEQ ID NO: 320)	455
HOOK2 PROTEIN (SEQ ID NO: 13)	TGTGTTAGGAATGATTGGGTA (SEQ ID NO: 322) AATTTCAAAACCAAAATCACC (SEQ ID NO: 323)	461
(SEQ ID NO: 14)	AATTACCAAACCAATTCCTCTTA (SEQ ID NO: 325) GGTTGGGATTTTAGTGTGTG (SEQ ID NO: 324)	366
(SEQ ID NO: 14)	TTATTTGAGGGATTTATTGGAG (SEQ ID NO: 326) CCTTATTAAAACTTACCACCCTAT (SEQ ID NO: 327)	382
(SEQ ID NO: 15)	GTGGGTTAGTGGGAGGTTAT (SEQ ID NO: 328) TAAAAACCCTTCCTACCTCTTA (SEQ ID NO: 329)	440
(SEQ ID NO: 16)	AGATGGGTATGTATTTTGGGTT (SEQ ID NO: 330) ACTAAACTCAACCACCTCACTAA (SEQ ID NO: 331)	181
(SEQ ID NO: 17)	TTTTGGTTAGTTTTATGGGGTA (SEQ ID NO: 332) CACTACTTCAAATCCATCATCA (SEQ ID NO: 333)	484

SEQ ID No:	*Primer:*	*Amplificate Length:*
LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN (RETINOIC ACID-INDUCIBLE E3 PROTEIN) (HA1520) LAM5 (SEQ ID NO: 18)	TAACTTCACAAATTACCCAACA (SEQ ID NO: 335) AAGAGTGAGGAGTAAGGGAGTT (SEQ ID NO: 334)	455
"TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE) (SEQ ID NO: 19)	TTTTGGGGTTAGTATGTGAGTT (SEQ ID NO: 336) ATCCCAACAACTTCTTCCTC (SEQ ID NO: 337)	482
PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	GAAGAGGAATGGAAAATTAG (SEQ ID NO: 338) TCACCAACAAAATACCCAA (SEQ ID NO: 339)	500
PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR,	AACCATCAACCATACCTATTTC (SEQ ID NO: 341) TGAGTAAGATGATTATTTGGATTT (SEQ ID NO: 340)	467

SEQ ID No:	Primer:	Amplificate Length:
EP4 SUBTYPE) (SEQ ID NO: 20)		
(SEQ ID NO: 21)	CACTTCCCACCTCCTTATATC (SEQ ID NO: 343) ATTGGGTTTGAAAGAGTTGTAG (SEQ ID NO: 342)	398
(SEQ ID NO: 22)	ATGATGGGAATATGTAAGAATGA (SEQ ID NO: 344) CTTCTCACTACTAATCTCCTACCC (SEQ ID NO: 345)	290
EQUILIBRATIVE NUCLEOSIDE TRANSPORTER 1 (EQUILIBRATIVE NITROBENZYLMERCAPTOPURINE RIBOSIDE-SENSITIVE NUCLEOSIDE TRANSPORTER) (EQUILIBRATIVE NBMPR-SENSITIVE NUCLEOSIDE TRANSPORTER) (NUCLEOSIDE TRANSPORTER, ES-TYPE (SEQ ID NO: 23)	GAGTTGGAGGGTTTTGTTTTA (SEQ ID NO: 346) CAAACTCCCATAAAATTCATCT (SEQ ID NO: 347)	410
ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN	CCACTCACTCAACCCATAA (SEQ ID NO: 349) GTGTGAGGTTTGGGTATTTTT (SEQ ID NO: 348)	398

SEQ ID No:	*Primer:*	*Amplificate Length:*
TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR) (SEQ ID NO: 24)		
PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN) (SEQ ID NO: 25)	GATGGTGGGTAGTGTTGTTTAT (SEQ ID NO: 350) AAAACCTATCTACACCTTTCTCTT (SEQ ID NO: 351)	378
(SEQ ID NO: 26)	ATTCCCACCAAAACCTCTAC (SEQ ID NO: 353) AATTAGAGAAGGTTAAATGGGTT (SEQ ID NO: 352)	300
(SEQ ID NO: 27)	AATAACTCCAACTTTCCTCCC (SEQ ID NO: 355) GGGATTTGGGAATTTATTGT (SEQ ID NO: 354)	237
(SEQ ID NO: 27)	GGTGGATGAGTAGTTTGAAGTTT (SEQ ID NO: 356) AAAAACCCCTTTCCCTCT (SEQ ID NO: 357)	427
(SEQ ID NO: 28)	GTTGGGGTTTAGTAATTGAAAA (SEQ ID NO: 358) ACCAACACAAACTAACACTTACAT	404

SEQ ID No:	Primer:	Amplificate Length:
	(SEQ ID NO: 359)	
PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	AAGAGGTTTTATGGTGTTTGAG (SEQ ID NO: 360) CACTCCCTTCCCAAACTATAC (SEQ ID NO: 361)	473
HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2) (SEQ ID NO: 30)	CTCCTCAATTCTCACCAAAA (SEQ ID NO: 363) GTGGAAAAAGGAGAGTAAATTG (SEQ ID NO: 362)	356
LIM DOMAIN KINASE 1 (EC 2.7.1.37) (LIMK-1) (SEQ ID NO: 31)	AAACCCTACTTCCTACAAACAA (SEQ ID NO: 365) AGGGAGGTTTGGTGTATTTT (SEQ ID NO: 364)	420
LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-	CAATCCCCTTAAAACAAACC (SEQ ID NO: 367) GGAAAGGATAGGATGTTGGAT (SEQ ID NO: 366)	500

SEQ ID No:	Primer:	Amplificate Length:
RIIA) (CD32) (CDW32) (SEQ ID NO: 32)		
1-ACYL-SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE GAMMA (EC 2.3.1.51) (1-AGP ACYLTRANSFERASE 3) (1-AGPAT 3) (LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-GAMMA) (LPAAT-GAMMA) (1-ACYLGLYCEROL-3-PHOSPHATE O-ACYLTRANSFERASE 3) (SEQ ID NO: 33)	CACAATTTCCCACAAAACA (SEQ ID NO: 369) TTAGGGAGATGAGATTAAAGGA (SEQ ID NO: 368)	379
HOMEOBOX PROTEIN GSH-2 (SEQ ID NO: 34)	TATATGGGGTGGGAGTATTTT (SEQ ID NO: 370) CCTTCCCCTCCTTCTTATACT (SEQ ID NO: 371)	276
(SEQ ID NO: 35)	AAAATTCTTTCCTCTCCTAAACA (SEQ ID NO: 373) TTAGGGGTTATTAGGTTAAATGA (SEQ ID NO: 372)	478
HISTONE H4 (SEQ ID NO: 36)	TTAGTTGAGAAAGTGGGGGT (SEQ ID NO: 374) CTACCTCAAACCAAAATCCTC (SEQ ID NO: 375)	421
POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY	TTTTGGAGTTATAGGGTTTTGT (SEQ ID NO: 376) CTTCAACATCTCCCAATCC (SEQ ID NO: 377)	441

SEQ ID No:	Primer:	Amplificate Length:
KQT MEMBER 2 (NEUROBLASTOMA-SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2) (SEQ ID NO: 37)		
ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22) (SEQ ID NO: 38)	AAACCTAAAAATCCAACACAAA (SEQ ID NO: 379) GGGTTATGTTAAGGGAGAAAG (SEQ ID NO: 378)	215
(SEQ ID NO: 39)	AATAACCTAATCTCCAAACCC (SEQ ID NO: 381) ATTTGTGGTAGTTAATAGGTATGTTTA (SEQ ID NO: 380)	465

SEQ ID No:	Primer:	Amplificate Length:
(SEQ ID NO: 40)	TACCCACCATATACCAAAACTAAA (SEQ ID NO: 383) TAGAGAAGTTGTTTGTTGGTTG (SEQ ID NO: 382)	484
PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	ATTTGAGGGGTATTATTTGTTG (SEQ ID NO: 384) AACCACCTTCTCCCCTAAT (SEQ ID NO: 385)	409
(SEQ ID NO: 42)	GTAATAATTGGGTTAGGGGTTA (SEQ ID NO: 386) AACCAATATCAAATAACTAAAATCC (SEQ ID NO: 387)	394
(SEQ ID NO: 43)	AAAATCCAATCCTAAAACCCTA (SEQ ID NO: 389) TATTTGAGAAAGTGGTAGGAGG (SEQ ID NO: 388)	296
(SEQ ID NO: 44)	AACCCTAACTTCTAAACAATTCC (SEQ ID NO: 391) TTTATGTTTGTTGGGGGTAGT (SEQ ID NO: 390)	492
(SEQ ID NO: 45)	ACCCCAATCAACTACATAACTAA (SEQ ID NO: 393) GTGAGAGTGGGTGTTGAAAT (SEQ ID NO: 392)	498
(SEQ ID NO: 46)	GAAGGTAGGTTAGTAAGAAGGGT (SEQ ID NO: 394) TACCTAATCCCCCAAAACA (SEQ ID NO: 395)	289
(SEQ ID NO: 47)	CACTCACTTAATCATCACCATC (SEQ ID NO: 397) GGAGGAGTTGGGAGTTAGTAT (SEQ ID NO: 396)	459
(SEQ ID NO: 48)	TGATTTGATTAGTTTGGTATTGTT (SEQ ID NO: 398) CAAACACCCCTTAACCCT (SEQ ID NO: 399)	454
(SEQ ID NO: 49)	TAGTGTGTTTGGTTAGAGTGGT (SEQ ID NO: 400) ACACATCTTAAACTTCCCCA (SEQ ID NO: 401)	249
DNA REPLICATIO	AACCAACACCTCCTAAACAAT (SEQ ID NO: 403)	412

SEQ ID No:	Primer:	Amplificate Length:
N FACTOR; DOUBLE PARKED, DROSOPHILA, HOMOLOG OF (SEQ ID NO: 50)	GTTGGGTTTATTTTGAGTTGAG (SEQ ID NO: 402)	
PR-DOMAIN ZINC FINGER PROTEIN 16 (TRANSCRIPTION FACTOR MEL1) (SEQ ID NO: 51)	TTGTTTGTTTTGAGTAAGAAGG (SEQ ID NO: 404) ATACCCCAATAACCACCTCTAT (SEQ ID NO: 405)	475
TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5;	ACCAATCTAAAAATCCCCAAC (SEQ ID NO: 407) GGTATTAGGAGGTAGAAGTGGA (SEQ ID NO: 406)	474

SEQ ID No:	Primer:	Amplificate Length:
IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)		
CDH1 (SEQ ID NO: 54)	GAGGTTGGGGTTAGAGGAT (SEQ ID NO: 408) CAAACTCACAAATACTTTACAATTC (SEQ ID NO: 409)	478
CD44 (SEQ ID NO: 56)	GAAAGGAGAGGTTAAAGGTTG (SEQ ID NO: 410) AACTCACTTAACTCCAATCCC (SEQ ID NO: 411)	696
GSTP1 (SEQ ID NO: 57)	CCTCTCCCCTACCCTATAAA (SEQ ID NO: 413) GTTGGTTTTATGTTGGGAGTT (SEQ ID NO: 412)	469
VIAAT (SEQ ID NO: 59)	CAAACCCAATTCTCAATATCC (SEQ ID NO: 415) GAAGTTGTTGTATATGAGGTTGTTA (SEQ ID NO: 414)	434

TABLE 9

No:	Gene	Oligo:
1	VIAAT (SEQ ID NO: 59)	TAGACGCGGACGTTTA (SEQ ID NO: 416)
2	VIAAT (SEQ ID NO: 59)	TAATTAGATGTGGATGTT (SEQ ID NO: 417)
3	VIAAT (SEQ ID NO: 59)	TTCGTATAGGTACGCGA (SEQ ID NO: 418)
4	VIAAT (SEQ ID NO: 59)	TTTTGTATAGGTATGTGA (SEQ ID NO: 419)
5	VIAAT (SEQ ID NO: 59)	TTCGTACGCGTATTAT (SEQ ID NO: 420)
6	VIAAT (SEQ ID NO: 59)	GAGTTTTGTATGTGTATT (SEQ ID NO: 421)
7	VIAAT (SEQ ID NO: 59)	TTCGGTCGTTTAGCGT (SEQ ID NO: 422)
8	VIAAT (SEQ ID NO: 59)	ATTTGGTTGTTTAGTGT (SEQ ID NO: 423)

No:	Gene	Oligo:
9	(SEQ ID NO: 1)	GTCGGTGGTTCGAGTA (SEQ ID NO: 424)
10	(SEQ ID NO: 1)	GTTGGTGGTTTGAGTAT (SEQ ID NO: 425)
11	(SEQ ID NO: 1)	GGAATTCGACGGGGAG (SEQ ID NO: 426)
12	(SEQ ID NO: 1)	GGGAATTTGATGGGGA (SEQ ID NO: 427)
13	(SEQ ID NO: 1)	TTCGTCGGGCGTTTAG (SEQ ID NO: 428)
14	(SEQ ID NO: 1)	TTTGTTGGGTGTTTAGT (SEQ ID NO: 429)
15	(SEQ ID NO: 1)	GTCGTTCGTCGATGTA (SEQ ID NO: 430)
16	(SEQ ID NO: 1)	GGTTGTTTGTTGATGTAG (SEQ ID NO: 431)
17	(SEQ ID NO: 2)	GTATTGCGCGTTTATT (SEQ ID NO: 432)
18	(SEQ ID NO: 2)	AGGGTATTGTGTGTTTA (SEQ ID NO: 433)
19	(SEQ ID NO: 2)	AGGTACGTGGCGTTTT (SEQ ID NO: 434)
20	(SEQ ID NO: 2)	AGGTATGTGGTGTTTT (SEQ ID NO: 435)
21	(SEQ ID NO: 2)	GAGTTGCGCGGTAGTT (SEQ ID NO: 436)
22	(SEQ ID NO: 2)	AGGAGTTGTGTGGTAG (SEQ ID NO: 437)
23	(SEQ ID NO: 2)	ATAGTTTTCGCGTTTT (SEQ ID NO: 438)
24	(SEQ ID NO: 2)	AGTTTTTGTGTTTTAGGA (SEQ ID NO: 439)
25	(SEQ ID NO: 3)	TTTCGGTCGCGAATAT (SEQ ID NO: 440)
26	(SEQ ID NO: 3)	TTTGGTTGTGAATATTTT (SEQ ID NO: 441)
27	(SEQ ID NO: 3)	GTCGAGAGTTCGCGTT (SEQ ID NO: 442)
28	(SEQ ID NO: 3)	TAGTTGAGAGTTTGTGT (SEQ ID NO: 443)
29	(SEQ ID NO: 3)	TTTCGGTACGACGTTT (SEQ ID NO: 444)
30	(SEQ ID NO: 3)	GAGTTTTGGTATGATGT (SEQ ID NO: 445)
31	(SEQ ID NO: 3)	ATTGGGCGCGGTTTAA (SEQ ID NO: 446)
32	(SEQ ID NO: 3)	ATTGGGTGTGGTTTAA (SEQ ID NO: 447)
33	LIM/HOMEOBOX PROTEIN LHX9	ATTGTCGGGATACGTT (SEQ ID NO: 448)

No:	Gene	Oligo:
	(SEQ ID NO: 4)	
34	LIM/HOMEOBOX PROTEIN LHX9 (SEQ ID NO: 4)	GATTGTTGGGATATGTT (SEQ ID NO: 449)
35	LIM/HOMEOBOX PROTEIN LHX9 (SEQ ID NO: 4)	TTAGTGTCGCGTTATT (SEQ ID NO: 450)
36	LIM/HOMEOBOX PROTEIN LHX9 (SEQ ID NO: 4)	AGTGTTGTGTTATTTGG (SEQ ID NO: 451)
37	LIM/HOMEOBOX PROTEIN LHX9 (SEQ ID NO: 4)	TGAAACGTTAGCGTTA (SEQ ID NO: 452)
38	LIM/HOMEOBOX PROTEIN LHX9 (SEQ ID NO: 4)	AGTGAAATGTTAGTGTT (SEQ ID NO: 453)
39	LIM/HOMEOBOX PROTEIN LHX9 (SEQ ID NO: 4)	AAAGGCGCGGTTTTTA (SEQ ID NO: 454)
40	LIM/HOMEOBOX PROTEIN LHX9 (SEQ ID NO: 4)	TTGAAAGGTGTGGTTT (SEQ ID NO: 455)
41	(SEQ ID NO: 5)	TAAGTAGCGGCGTTGT (SEQ ID NO: 456)
42	(SEQ ID NO: 5)	TAAGTAGTGGTGTTGTA (SEQ ID NO: 457)
43	(SEQ ID NO: 5)	GAGATGAGCGTCGTGG (SEQ ID NO: 458)
44	(SEQ ID NO: 5)	GAGATGAGTGTTGTGG (SEQ ID NO: 459)
45	(SEQ ID NO: 5)	GTCGTTCGTTAGTAACGG (SEQ ID NO: 460)
46	(SEQ ID NO: 5)	GTTGTTTGTTAGTAATGG (SEQ ID NO: 461)
47	(SEQ ID NO: 5)	TATCGGTTTTCGCGGT (SEQ ID NO: 462)
48	(SEQ ID NO: 5)	ATATTGGTTTTTGTGGT (SEQ ID NO: 463)
49	(SEQ ID NO: 5)	TTGGACGGCGTGTATT (SEQ ID NO: 464)
50	(SEQ ID NO: 5)	TTTGGATGGTGTGTAT (SEQ ID NO: 465)
51	(SEQ ID NO: 6)	GACGTTGTCGTAATGA (SEQ ID NO: 466)
52	(SEQ ID NO: 6)	TGATGTTGTTGTAATGA (SEQ ID NO: 467)
53	(SEQ ID NO: 6)	AGTATACGAGACGCGA (SEQ ID NO: 468)
54	(SEQ ID NO: 6)	AGAGTATATGAGATGTGA (SEQ ID NO: 469)

No:	Gene	Oligo:
55	(SEQ ID NO: 6)	TTCGTTTATCGTGCGG (SEQ ID NO: 470)
56	(SEQ ID NO: 6)	TTTGTTTATTGTGTGGT (SEQ ID NO: 471)
57	(SEQ ID NO: 6)	AGGACGTAGAGCGTAG (SEQ ID NO: 472)
58	(SEQ ID NO: 6)	TGAGGATGTAGAGTGT (SEQ ID NO: 473)
59	(SEQ ID NO: 7)	TATAGACGGTGGGCGA (SEQ ID NO: 474)
60	(SEQ ID NO: 7)	TATAGATGGTGGGTGA (SEQ ID NO: 475)
61	(SEQ ID NO: 7)	ATTTATCGCGGTGGTT (SEQ ID NO: 476)
62	(SEQ ID NO: 7)	GGATTTATTGTGGTGG (SEQ ID NO: 477)
63	(SEQ ID NO: 7)	ATTCGTTGATTCGCGG (SEQ ID NO: 478)
64	(SEQ ID NO: 7)	TTTGTTGATTTGTGGGG (SEQ ID NO: 479)
65	UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN) (SEQ ID NO: 8)	TTTAGTCGATTCGGGA (SEQ ID NO: 480)
66	UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-	AGTTGATTTGGGAGAA (SEQ ID NO: 481)

No:	Gene	Oligo:
	1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN) (SEQ ID NO: 8)	
67	UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN) (SEQ ID NO: 8)	TGAGCGAGTTCGGAGA (SEQ ID NO: 482)
68	UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN) (SEQ ID NO: 8)	GATGAGTGAGTTTGGA (SEQ ID NO: 483)
69	UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE	TTTCGGGAGTTTCGTA (SEQ ID NO: 484)

No:	Gene	Oligo:
	PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN) (SEQ ID NO: 8)	
70	UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN) (SEQ ID NO: 8)	TTTGGGAGTTTTGTAGT (SEQ ID NO: 485)
71	UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN) (SEQ ID NO: 8)	TTTCGGTCGTAGTCGG (SEQ ID NO: 486)
72	UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-	ATTTTTGGTTGTAGTTGG (SEQ ID NO: 487)

No:	Gene	Oligo:
	HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN) (SEQ ID NO: 8)	
73	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	ATTGAGTTCGGGTTCGT (SEQ ID NO: 488)
74	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	ATTGAGTTTGGGTTTGT (SEQ ID NO: 489)
75	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	TAGCGTATATGCGATT (SEQ ID NO: 490)
76	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	GGGTAGTGTATATGTGA (SEQ ID NO: 491)
77	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	ATATGCGATTGATTTTACGG (SEQ ID NO: 492)
78	BASSOON; ZINC	ATATGTGATTGATTTTATGG

No:	Gene	Oligo:
	FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	(SEQ ID NO: 493)
79	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	TTATAGCGTCGTATGG (SEQ ID NO: 494)
80	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	ATAGTGTTGTATGGGAA (SEQ ID NO: 495)
81	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	GACGTAGGTTCGTGAT (SEQ ID NO: 496)
82	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	ATGATGTAGGTTTGTGA (SEQ ID NO: 497)
83	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	GGTAGCGTTTATTCGT (SEQ ID NO: 498)
84	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	AGGTAGTGTTTATTTGTA (SEQ ID NO: 499)
85	BASSOON; ZINC FINGER PROTEIN	ATAGTCGAGTTTCGTT (SEQ ID NO: 500)

No:	Gene	Oligo:
	231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	
86	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	GTTGAGTTTTGTTTAGG (SEQ ID NO: 501)
87	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	TGGGTATACGTGTTAG (SEQ ID NO: 502)
88	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	TATGGGTATATGTGTTAG (SEQ ID NO: 503)
89	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	TTAGATGCGTAAGGTT (SEQ ID NO: 504)
90	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	ATTAGATGTGTAAGGTTT (SEQ ID NO: 505)
91	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	TTATGGGTCGTAGGAT (SEQ ID NO: 506)
92	BASSOON; ZINC FINGER PROTEIN 231; NEURONAL	ATGGGTTGTAGGATTG (SEQ ID NO: 507)

No:	Gene	Oligo:
	DOUBLE ZINC FINGER PROTEIN (SEQ ID NO: 9)	
93	(SEQ ID NO: 10)	TTCGTTTAGTTACGTACGG (SEQ ID NO: 508)
94	(SEQ ID NO: 10)	TTTGTTTAGTTATGTATGG (SEQ ID NO: 509)
95	(SEQ ID NO: 10)	TAGTTACGTACGGATAT (SEQ ID NO: 510)
96	(SEQ ID NO: 10)	TTATGTATGGATATTTTGG (SEQ ID NO: 511)
97	(SEQ ID NO: 10)	AGGATACGTAGTTCGT (SEQ ID NO: 512)
98	(SEQ ID NO: 10)	AGGATATGTAGTTTGTATA (SEQ ID NO: 513)
99	(SEQ ID NO: 10)	AGTTCGTATATTTTCGG (SEQ ID NO: 514)
100	(SEQ ID NO: 10)	AGTTTGTATATTTTTGGTA (SEQ ID NO: 515)
101	(SEQ ID NO: 11)	TACGGGGTCGTTCGTA (SEQ ID NO: 516)
102	(SEQ ID NO: 11)	TATGGGGTTGTTTGTAT (SEQ ID NO: 517)
103	(SEQ ID NO: 11)	TTCGTAGGCGATCGTA (SEQ ID NO: 518)
104	(SEQ ID NO: 11)	GATTTGTAGGTGATTGT (SEQ ID NO: 519)
105	(SEQ ID NO: 11)	TAGCGGTCGATTCGTT (SEQ ID NO: 520)
106	(SEQ ID NO: 11)	TAGTGGTTGATTTGTTT (SEQ ID NO: 521)
107	(SEQ ID NO: 11)	GTCGTTACGTTTTTCGG (SEQ ID NO: 522)
108	(SEQ ID NO: 11)	TAGAGTTGTTATGTTTTTTGG (SEQ ID NO: 523)
109	(SEQ ID NO: 12)	AAGTTCGTTACGGCGG (SEQ ID NO: 524)
110	(SEQ ID NO: 12)	AGTTTGTTATGGTGGG (SEQ ID NO: 525)
111	(SEQ ID NO: 12)	TACGTTGGTCGACGTT (SEQ ID NO: 526)
112	(SEQ ID NO: 12)	TTTATGTTGGTTGATGT (SEQ ID NO: 527)
113	(SEQ ID NO: 12)	GAGTCGGACGGTGTTT (SEQ ID NO: 528)
114	(SEQ ID NO: 12)	GAGTTGGATGGTGTTT (SEQ ID NO: 529)
115	HOOK2 PROTEIN	TAGCGTAAAGGGACGAG (SEQ ID NO: 530)

No:	Gene	Oligo:
	(SEQ ID NO: 13)	
116	HOOK2 PROTEIN (SEQ ID NO: 13)	TAGTGTAAAGGGATGAG (SEQ ID NO: 531)
117	HOOK2 PROTEIN (SEQ ID NO: 13)	ATGCGGATATTTCGTT (SEQ ID NO: 532)
118	HOOK2 PROTEIN (SEQ ID NO: 13)	GGATGTGGATATTTTGT (SEQ ID NO: 533)
119	HOOK2 PROTEIN (SEQ ID NO: 13)	ATTTCGTTTTCGGAGT (SEQ ID NO: 534)
120	HOOK2 PROTEIN (SEQ ID NO: 13)	GGATATTTTGTTTTTGGA (SEQ ID NO: 535)
121	HOOK2 PROTEIN (SEQ ID NO: 13)	AGGTAGCGTAAAGGGA (SEQ ID NO: 536)
122	HOOK2 PROTEIN (SEQ ID NO: 13)	AGGTAGTGTAAAGGGA (SEQ ID NO: 537)
123	(SEQ ID NO: 14)	TAACGTATCGTTAGGG (SEQ ID NO: 538)
124	(SEQ ID NO: 14)	AATGTATTGTTAGGGATG (SEQ ID NO: 539)
125	(SEQ ID NO: 14)	TTTTTGGCGCGGAGTA (SEQ ID NO: 540)
126	(SEQ ID NO: 14)	TTTTGGTGTGGAGTAG (SEQ ID NO: 541)
127	(SEQ ID NO: 14)	TAGAGTTCGACGGGTT (SEQ ID NO: 542)
128	(SEQ ID NO: 14)	AGAGTTTGATGGGTTT (SEQ ID NO: 543)
129	(SEQ ID NO: 14)	ATCGAATTTATCGGTCGG (SEQ ID NO: 544)
130	(SEQ ID NO: 14)	ATTGAATTTATTGGTTGG (SEQ ID NO: 545)
131	(SEQ ID NO: 14)	TATTACGGGGAACGGT (SEQ ID NO: 546)
132	(SEQ ID NO: 14)	TATTATGGGGAATGGTT (SEQ ID NO: 547)
133	(SEQ ID NO: 14)	GAACGGTTCGTTTTTA (SEQ ID NO: 548)
134	(SEQ ID NO: 14)	GGGAATGGTTTGTTTT (SEQ ID NO: 549)
135	(SEQ ID NO: 14)	AAGGGGATCGTTTTTT (SEQ ID NO: 550)
136	(SEQ ID NO: 14)	TAAGGGGATTGTTTTTT (SEQ ID NO: 551)

No:	Gene	Oligo:
137	(SEQ ID NO: 14)	TTTTAGGGCGGTTTAA (SEQ ID NO: 552)
138	(SEQ ID NO: 14)	TTAGGGTGGTTTAAGG (SEQ ID NO: 553)
139	(SEQ ID NO: 15)	TGACGAAAATCGATTG (SEQ ID NO: 554)
140	(SEQ ID NO: 15)	GATGAAAATTGATTGGAT (SEQ ID NO: 555)
141	(SEQ ID NO: 15)	GGGTATACGAATACGT (SEQ ID NO: 556)
142	(SEQ ID NO: 15)	GTGGGTATATGAATATGT (SEQ ID NO: 557)
143	(SEQ ID NO: 15)	TTCGAGGTTACGGGTT (SEQ ID NO: 558)
144	(SEQ ID NO: 15)	TTTGAGGTTATGGGTT (SEQ ID NO: 559)
145	(SEQ ID NO: 15)	TGTTCGAGGTATATACGT (SEQ ID NO: 560)
146	(SEQ ID NO: 15)	TTGTTTGAGGTATATATGT (SEQ ID NO: 561)
147	(SEQ ID NO: 16)	AGGAGATTCGGTTATAT (SEQ ID NO: 562)
148	(SEQ ID NO: 16)	GAGGAGATTTGGTTATAT (SEQ ID NO: 563)
149	(SEQ ID NO: 16)	GTTATTTTCGGTAATGTT (SEQ ID NO: 564)
150	(SEQ ID NO: 16)	AGGTTATTTTTGGTAATG (SEQ ID NO: 565)
151	(SEQ ID NO: 16)	TATTAGTCGTTAGTTTGA (SEQ ID NO: 566)
152	(SEQ ID NO: 16)	TATTAGTTGTTAGTTTGAG (SEQ ID NO: 567)
153	(SEQ ID NO: 16)	AGGTTTATACGATAAAGG (SEQ ID NO: 568)
154	(SEQ ID NO: 16)	AGGTTTATATGATAAAGGT (SEQ ID NO: 569)
155	(SEQ ID NO: 17)	TTCGAATATTAGCGCGT (SEQ ID NO: 570)
156	(SEQ ID NO: 17)	ATTTTGAATATTAGTGTGT (SEQ ID NO: 571)
157	(SEQ ID NO: 17)	TTTATGAGCGGCGAGT (SEQ ID NO: 572)
158	(SEQ ID NO: 17)	GAGTGGTGAGTTTAGG (SEQ ID NO: 573)
159	(SEQ ID NO: 17)	AGTCGGTAACGCGTAT (SEQ ID NO: 574)
160	(SEQ ID NO: 17)	AGAGTTGGTAATGTGTA (SEQ ID NO: 575)
161	(SEQ ID NO: 17)	TTTTTTACGCGGAAGG (SEQ ID NO: 576)

No:	Gene	Oligo:
162	(SEQ ID NO: 17)	TTTTATGTGGAAGGGG (SEQ ID NO: 577)
163	LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN (RETINOIC ACID-INDUCIBLE E3 PROTEIN) (HA1520) LAM5 (SEQ ID NO: 18)	AGGTCGGTCGTAGATA (SEQ ID NO: 578)
164	LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN (RETINOIC ACID-INDUCIBLE E3 PROTEIN) (HA1520) LAM5 (SEQ ID NO: 18)	GAGGTTGGTTGTAGAT (SEQ ID NO: 579)
165	LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN (RETINOIC ACID-INDUCIBLE E3 PROTEIN) (HA1520) LAM5 (SEQ ID NO: 18)	GACGTTTATTTCGAGG (SEQ ID NO: 580)
166	LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN (RETINOIC ACID-INDUCIBLE E3 PROTEIN) (HA1520) LAM5 (SEQ ID NO: 18)	TGATGTTTATTTTGAGGT (SEQ ID NO: 581)
167	LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE	TTTGATCGGGATGTGA (SEQ ID NO: 582)

No:	Gene	Oligo:
	PROTEIN (RETINOIC ACID-INDUCIBLE E3 PROTEIN) (HA1520) LAM5 (SEQ ID NO: 18)	
168	LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN (RETINOIC ACID-INDUCIBLE E3 PROTEIN) (HA1520) LAM5 (SEQ ID NO: 18)	TTTGATTGGGATGTGA (SEQ ID NO: 583)
169	LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN (RETINOIC ACID-INDUCIBLE E3 PROTEIN) (HA1520) LAM5 (SEQ ID NO: 18)	TGTAATTGACGTTTATTT (SEQ ID NO: 584)
170	LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN (RETINOIC ACID-INDUCIBLE E3 PROTEIN) (HA1520) LAM5 (SEQ ID NO: 18)	AATGTAATTGATGTTTATTT (SEQ ID NO: 585)
171	"TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE) (SEQ ID NO: 19)	ATCGGTGTTAGCGGAT (SEQ ID NO: 586)
172	"TYPE I INOSITOL-1,4,5-TRISPHOSPHATE	AATTGGTGTTAGTGGA (SEQ ID NO: 587)

No:	Gene	Oligo:
	5-PHOSPHATASE (EC 3.1.3.56) (5PTASE) (SEQ ID NO: 19)	
173	"TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE) (SEQ ID NO: 19)	ATGTTCGTAGGTGTCGG (SEQ ID NO: 588)
174	"TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE) (SEQ ID NO: 19)	TTTGTAGGTGTTGGGTA (SEQ ID NO: 589)
175	"TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE) (SEQ ID NO: 19)	GTCGTTGTTATCGAGG (SEQ ID NO: 590)
176	"TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE) (SEQ ID NO: 19)	GGTTGTTGTTATTGAGG (SEQ ID NO: 591)
177	"TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE) (SEQ ID NO: 19)	ATTGCGGTTTTATCGG (SEQ ID NO: 592)
178	"TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE) (SEQ ID NO: 19)	ATTGTGGTTTTATTGGT (SEQ ID NO: 593)
179	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID	TTCGATCGGTTGAATA (SEQ ID NO: 594)

No:	Gene	Oligo:
	EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	
180	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	TTGAGTTTTGATTGGTT (SEQ ID NO: 595)
181	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	TAAGTCGCGTAAGGAG (SEQ ID NO: 596)
182	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	AAGTTGTGTAAGGAGTA (SEQ ID NO: 597)
183	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	AGGTTCGTTAATCGTT (SEQ ID NO: 598)
184	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	TGAGGTTTGTTAATTGT (SEQ ID NO: 599)

No:	*Gene*	*Oligo:*
185	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	TACGTTGGACGTATAG (SEQ ID NO: 600)
186	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	AGAGTATGTTGGATGTA (SEQ ID NO: 601)
187	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	AGTCGCGAGTTATCGA (SEQ ID NO: 602)
188	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	AGTTGTGAGTTATTGAG (SEQ ID NO: 603)
189	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	TAGCGCGTCGTATATA (SEQ ID NO: 604)
190	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR)	GGAGTAGTGTGTTGTAT (SEQ ID NO: 605)

No:	Gene	Oligo:
	(PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	
191	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	GTCGAAAGTCGTTGAG (SEQ ID NO: 606)
192	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	GTTGAAAGTTGTTGAGG (SEQ ID NO: 607)
193	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	TAGGACGTATCGCGAG (SEQ ID NO: 608)
194	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	TAGGATGTATTGTGAGT (SEQ ID NO: 609)
195	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	AGTGTATCGTTTTTCGG (SEQ ID NO: 610)
196	PROSTAGLANDIN	TAGTGTATTGTTTTTTGG

No:	Gene	Oligo:
	E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	(SEQ ID NO: 611)
197	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	TTCGTTTACGGTAGTT (SEQ ID NO: 612)
198	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	ATTTTTGTTTATGGTAGTT (SEQ ID NO: 613)
199	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	TGCGTATCGTTAGTTA (SEQ ID NO: 614)
200	PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE) (SEQ ID NO: 20)	AGGTTGTGTATTGTTAG (SEQ ID NO: 615)
201	(SEQ ID NO: 21)	ATTCGGCGAATAGTAG (SEQ ID NO: 616)
202	(SEQ ID NO: 21)	TATTTGGTGAATAGTAGTA (SEQ ID NO: 617)
203	(SEQ ID NO: 21)	ATAGCGTTGGTCGTTA (SEQ ID NO: 618)

No:	Gene	Oligo:
204	(SEQ ID NO: 21)	ATAGTGTTGGTTGTTAG (SEQ ID NO: 619)
205	(SEQ ID NO: 21)	TTCGGGATACGAGTTT (SEQ ID NO: 620)
206	(SEQ ID NO: 21)	GTTTGGGATATGAGTTT (SEQ ID NO: 621)
207	(SEQ ID NO: 21)	TACGATAAGTCGGAGA (SEQ ID NO: 622)
208	(SEQ ID NO: 21)	GGGTTATGATAAGTTGG (SEQ ID NO: 623)
209	(SEQ ID NO: 22)	TATCGGCGAGTTGTAT (SEQ ID NO: 624)
210	(SEQ ID NO: 22)	GGTTATTGGTGAGTTG (SEQ ID NO: 625)
211	(SEQ ID NO: 22)	TTAACGTTTGGGGACGT (SEQ ID NO: 626)
212	(SEQ ID NO: 22)	TTAATGTTTGGGGATGT (SEQ ID NO: 627)
213	(SEQ ID NO: 22)	TATTCGCGTTTTTAGAT (SEQ ID NO: 628)
214	(SEQ ID NO: 22)	TTATTTGTGTTTTTAGATTA (SEQ ID NO: 629)
215	EQUILIBRATIVE NUCLEOSIDE TRANSPORTER 1 (EQUILIBRATIVE NITROBENZYLMERCAPTOPURINE RIBOSIDE-SENSITIVE NUCLEOSIDE TRANSPORTER) (EQUILIBRATIVE NBMPR-SENSITIVE NUCLEOSIDE TRANSPORTER) (NUCLEOSIDE TRANSPORTER, ES-TYPE (SEQ ID NO: 23)	AGGGATAACGGAATATT (SEQ ID NO: 630)
216	EQUILIBRATIVE NUCLEOSIDE TRANSPORTER 1 (EQUILIBRATIVE NITROBENZYLMERCAPTOPURINE RIBOSIDE-SENSITIVE NUCLEOSIDE	GAAGGGATAATGGAATAT (SEQ ID NO: 631)

No:	Gene	Oligo:
	TRANSPORTER) (EQUILIBRATIVE NBMPR-SENSITIVE NUCLEOSIDE TRANSPORTER) (NUCLEOSIDE TRANSPORTER, ES-TYPE (SEQ ID NO: 23)	
217	EQUILIBRATIVE NUCLEOSIDE TRANSPORTER 1 (EQUILIBRATIVE NITROBENZYLMERCAPTOPURINE RIBOSIDE-SENSITIVE NUCLEOSIDE TRANSPORTER) (EQUILIBRATIVE NBMPR-SENSITIVE NUCLEOSIDE TRANSPORTER) (NUCLEOSIDE TRANSPORTER, ES-TYPE (SEQ ID NO: 23)	GAATAGTTTCGAGATGA (SEQ ID NO: 632)
218	EQUILIBRATIVE NUCLEOSIDE TRANSPORTER 1 (EQUILIBRATIVE NITROBENZYLMERCAPTOPURINE RIBOSIDE-SENSITIVE NUCLEOSIDE TRANSPORTER) (EQUILIBRATIVE NBMPR-SENSITIVE NUCLEOSIDE TRANSPORTER) (NUCLEOSIDE TRANSPORTER, ES-TYPE (SEQ ID NO: 23)	GGAATAGTTTTGAGATGA (SEQ ID NO: 633)
219	ORPHAN NUCLEAR	TTTTCGACGAAGTTTT (SEQ ID NO: 634)

No:	Gene	Oligo:
	RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR) (SEQ ID NO: 24)	
220	ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR) (SEQ ID NO: 24)	TTTTGATGAAGTTTTGTT (SEQ ID NO: 635)
221	ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR) (SEQ ID NO: 24)	TTACGGAGGCGTTTTA (SEQ ID NO: 636)
222	ORPHAN	TTTTATGGAGGTGTTTT

No:	Gene	Oligo:
	NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR) (SEQ ID NO: 24)	(SEQ ID NO: 637)
223	ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR) (SEQ ID NO: 24)	AGGCGAATTTATCGGG (SEQ ID NO: 638)
224	ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR) (SEQ ID NO: 24)	GGTGAATTTATTGGGG (SEQ ID NO: 639)

No:	Gene	Oligo:
225	ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR) (SEQ ID NO: 24)	TAGTCGAAGTAGGCGT (SEQ ID NO: 640)
226	ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR) (SEQ ID NO: 24)	TAGTTGAAGTAGGTGTT (SEQ ID NO: 641)
227	PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN) (SEQ ID NO: 25)	TTCGATCGAAGGTAAT (SEQ ID NO: 642)
228	PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC	TTTGTTTGATTGAAGGT (SEQ ID NO: 643)

No:	Gene	Oligo:
	3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN) (SEQ ID NO: 25)	
229	PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN) (SEQ ID NO: 25)	AGGCGATCGATATTAG (SEQ ID NO: 644)
230	PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN) (SEQ ID NO: 25)	GGTGATTGATATTAGGG (SEQ ID NO: 645)
231	PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN) (SEQ ID NO: 25)	TTAGCGTTCGTCGTTA (SEQ ID NO: 646)
232	PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL	TAATTAGTGTTTGTTGTTA (SEQ ID NO: 647)

No:	Gene	Oligo:
	AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN) (SEQ ID NO: 25)	
233	PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN) (SEQ ID NO: 25)	ATCGGTTCGGGAATTT (SEQ ID NO: 648)
234	PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN) (SEQ ID NO: 25)	AGATTGGTTTGGGAAT (SEQ ID NO: 649)
235	(SEQ ID NO: 26)	GTCGATTTCGTTACGG (SEQ ID NO: 650)
236	(SEQ ID NO: 26)	GTTGATTTTGTTATGGG (SEQ ID NO: 651)
237	(SEQ ID NO: 26)	TTCGGGTTTCGTATTA (SEQ ID NO: 652)
238	(SEQ ID NO: 26)	TTTTGGGTTTTGTATTAG (SEQ ID NO: 653)
239	(SEQ ID NO: 26)	AATTCGCGGTTTCGAT (SEQ ID NO: 654)
240	(SEQ ID NO: 26)	AATTTGTGGTTTTGATG (SEQ ID NO: 655)
241	(SEQ ID NO: 26)	GTCGTTTCGCGGAGAT (SEQ ID NO: 656)
242	(SEQ ID NO: 26)	GTTGTTTTGTGGAGATT (SEQ ID NO: 657)
243	(SEQ ID NO: 27)	ATTGGTCGATTCGCGG (SEQ ID NO: 658)
244	(SEQ ID NO: 27)	TATTGGTTGATTTGTGG (SEQ ID NO: 659)

No:	Gene	Oligo:
245	(SEQ ID NO: 27)	AGCGTTTCGATTTCGG (SEQ ID NO: 660)
246	(SEQ ID NO: 27)	AGTGTTTTGATTTTGGT (SEQ ID NO: 661)
247	(SEQ ID NO: 27)	ATCGAGCGTTTCGATT (SEQ ID NO: 662)
248	(SEQ ID NO: 27)	GGATTGAGTGTTTTGAT (SEQ ID NO: 663)
249	(SEQ ID NO: 27)	ATTCGCGTATTCGAGA (SEQ ID NO: 664)
250	(SEQ ID NO: 27)	TTTGTGTATTTGAGAGG (SEQ ID NO: 665)
251	(SEQ ID NO: 27)	GACGTTCGCGATTAAA (SEQ ID NO: 666)
252	(SEQ ID NO: 27)	TGGATGTTTGTGATTAA (SEQ ID NO: 667)
253	(SEQ ID NO: 27)	AAGTCGATATCGCGGT (SEQ ID NO: 668)
254	(SEQ ID NO: 27)	AAAAGTTGATATTGTGGT (SEQ ID NO: 669)
255	(SEQ ID NO: 27)	AGCGTTCGGAAGTTTA (SEQ ID NO: 670)
256	(SEQ ID NO: 27)	GGAGTGTTTGGAAGTT (SEQ ID NO: 671)
257	(SEQ ID NO: 27)	TATTCGGACGGGATA (SEQ ID NO: 672)
258	(SEQ ID NO: 27)	ATTTGGATGGGGATAG (SEQ ID NO: 673)
259	(SEQ ID NO: 27)	GAGACGCGTAGGTTAT (SEQ ID NO: 674)
260	(SEQ ID NO: 27)	GGGAGATGTGTAGGTT (SEQ ID NO: 675)
261	(SEQ ID NO: 28)	TAGTTTTCGGCGAAGG (SEQ ID NO: 676)
262	(SEQ ID NO: 28)	GGTAGTTTTTGGTGAAG (SEQ ID NO: 677)
263	(SEQ ID NO: 28)	AAGGCGGTGACGTAAA (SEQ ID NO: 678)
264	(SEQ ID NO: 28)	AAGGTGGTGATGTAAA (SEQ ID NO: 679)
265	(SEQ ID NO: 28)	ATGGCGTAAGTACGTT (SEQ ID NO: 680)
266	(SEQ ID NO: 28)	GATGGTGTAAGTATGTT (SEQ ID NO: 681)
267	(SEQ ID NO: 28)	AGTACGTTCGGGACGA (SEQ ID NO: 682)
268	(SEQ ID NO: 28)	AAGTATGTTTGGGATGA (SEQ ID NO: 683)
269	PEROXISOMAL MEMBRANE	ATGGTATTCGGGTCGT (SEQ ID NO: 684)

No:	Gene	Oligo:
	PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	
270	PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	TATGGTATTTGGGTTGT (SEQ ID NO: 685)
271	PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	TTGGAGCGTTAAGTAA (SEQ ID NO: 686)
272	PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	TATTTGGAGTGTTAAGTA (SEQ ID NO: 687)
273	PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14)	TGAAAGATTCGTTTGTT (SEQ ID NO: 688)

No:	Gene	Oligo:
	(PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	
274	PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	GTGAAAGATTTGTTTGTT (SEQ ID NO: 689)
275	PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	TGTATAACGAGAGGTG (SEQ ID NO: 690)
276	PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	TGTATAATGAGAGGTGA (SEQ ID NO: 691)
277	PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE	ATGTTTCGGGTATGGA (SEQ ID NO: 692)

No:	Gene	Oligo:
	ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	
278	PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN) (SEQ ID NO: 29)	ATGTTTTGGGTATGGA (SEQ ID NO: 693)
279	HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2) (SEQ ID NO: 30)	TTTTCGAGGAATTCGT (SEQ ID NO: 694)
280	HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2) (SEQ ID NO: 30)	TTTTTTGAGGAATTTGTT (SEQ ID NO: 695)
281	HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2) (SEQ ID NO: 30)	ATAGTTTTCGGCGGGT (SEQ ID NO: 696)
282	HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2) (SEQ ID NO: 30)	TATAGTTTTTGGTGGGT (SEQ ID NO: 697)
283	HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2) (SEQ ID NO: 30)	TTTTTCGGCGTAGATA (SEQ ID NO: 698)
284	HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2) (SEQ ID NO: 30)	TGTTTTTTGGTGTAGAT (SEQ ID NO: 699)
285	HOMEOBOX PROTEIN HOX-B6	TTACGGGCGTTAGAGA (SEQ ID NO: 700)

No:	Gene	Oligo:
	(HOX-2B) (HOX-2.2) (SEQ ID NO: 30)	
286	HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2) (SEQ ID NO: 30)	GGAGTTATGGGTGTTA (SEQ ID NO: 701)
287	LIM DOMAIN KINASE 1 (EC 2.7.1.37) (LIMK-1) (SEQ ID NO: 31)	TATCGGATTATCGCGG (SEQ ID NO: 702)
288	LIM DOMAIN KINASE 1 (EC 2.7.1.37) (LIMK-1) (SEQ ID NO: 31)	ATTGGATTATTGTGGGG (SEQ ID NO: 703)
289	LIM DOMAIN KINASE 1 (EC 2.7.1.37) (LIMK-1) (SEQ ID NO: 31)	GTCGGTAGTTTATCGGAT (SEQ ID NO: 704)
290	LIM DOMAIN KINASE 1 (EC 2.7.1.37) (LIMK-1) (SEQ ID NO: 31)	GTTGGTAGTTTATTGGAT (SEQ ID NO: 705)
291	LIM DOMAIN KINASE 1 (EC 2.7.1.37) (LIMK-1) (SEQ ID NO: 31)	TAGGAGACGTTACGTT (SEQ ID NO: 706)
292	LIM DOMAIN KINASE 1 (EC 2.7.1.37) (LIMK-1) (SEQ ID NO: 31)	AGATGTTATGTTAGGGT (SEQ ID NO: 707)
293	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32)	AAGAACGGACGTGTTT (SEQ ID NO: 708)

No:	Gene	Oligo:
	(SEQ ID NO: 32)	
294	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32) (SEQ ID NO: 32)	AGGAAGAATGGATGTG (SEQ ID NO: 709)
295	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32) (SEQ ID NO: 32)	TTTTTGCGATAGTCGG (SEQ ID NO: 710)
296	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32) (SEQ ID NO: 32)	GTTTTTGTGATAGTTGG (SEQ ID NO: 711)
297	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-	TAGCGGCGATTTAAGG (SEQ ID NO: 712)

No:	Gene	Oligo:
	RIIA) (CD32) (CDW32) (SEQ ID NO: 32)	
298	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32) (SEQ ID NO: 32)	GTAGTGGTGATTTAAGG (SEQ ID NO: 713)
299	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32) (SEQ ID NO: 32)	TTTACGAGCGAGTCGT (SEQ ID NO: 714)
300	LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32) (SEQ ID NO: 32)	TTTTATGAGTGAGTTGTT (SEQ ID NO: 715)
301	1-ACYL-SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE GAMMA (EC 2.3.1.51) (1- AGP ACYLTRANSFERASE 3) (1-AGPAT	TTTCGATAGTATACGGG (SEQ ID NO: 716)

No:	Gene	Oligo:
	3) (LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-GAMMA) (LPAAT-GAMMA) (1-ACYLGLYCEROL-3-PHOSPHATE O-ACYLTRANSFERASE 3) (SEQ ID NO: 33)	
302	1-ACYL-SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE GAMMA (EC 2.3.1.51) (1- AGP ACYLTRANSFERASE 3) (1-AGPAT 3) (LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-GAMMA) (LPAAT-GAMMA) (1-ACYLGLYCEROL-3-PHOSPHATE O-ACYLTRANSFERASE 3) (SEQ ID NO: 33)	TTTGATAGTATATGGGGA (SEQ ID NO: 717)
303	1-ACYL-SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE GAMMA (EC 2.3.1.51) (1- AGP ACYLTRANSFERASE 3) (1-AGPAT 3) (LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-GAMMA) (LPAAT-GAMMA) (1-ACYLGLYCEROL-3-PHOSPHATE O-ACYLTRANSFER	AAGGGAGCGTTCGTTA (SEQ ID NO: 718)

No:	Gene	Oligo:
	ASE 3) (SEQ ID NO: 33)	
304	1-ACYL-SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE GAMMA (EC 2.3.1.51) (1- AGP ACYLTRANSFERASE 3) (1-AGPAT 3) (LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-GAMMA) (LPAAT-GAMMA) (1-ACYLGLYCEROL-3-PHOSPHATE O-ACYLTRANSFERASE 3) (SEQ ID NO: 33)	AAGGGAGTGTTTGTTA (SEQ ID NO: 719)
305	1-ACYL-SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE GAMMA (EC 2.3.1.51) (1- AGP ACYLTRANSFERASE 3) (1-AGPAT 3) (LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-GAMMA) (LPAAT-GAMMA) (1-ACYLGLYCEROL-3-PHOSPHATE O-ACYLTRANSFERASE 3) (SEQ ID NO: 33)	AATAATAGCGACGGGG (SEQ ID NO: 720)
306	1-ACYL-SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE GAMMA (EC 2.3.1.51) (1- AGP ACYLTRANSFERASE 3) (1-AGPAT	TAATAGTGATGGGGGT (SEQ ID NO: 721)

No:	Gene	Oligo:
	3) (LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-GAMMA) (LPAAT-GAMMA) (1-ACYLGLYCEROL-3-PHOSPHATE O-ACYLTRANSFERASE 3) (SEQ ID NO: 33)	
307	HOMEOBOX PROTEIN GSH-2 (SEQ ID NO: 34)	TTTAGAATCGTCGAGT (SEQ ID NO: 722)
308	HOMEOBOX PROTEIN GSH-2 (SEQ ID NO: 34)	AGAATTGTTGAGTGAAG (SEQ ID NO: 723)
309	HOMEOBOX PROTEIN GSH-2 (SEQ ID NO: 34)	TTTTTCGTCGGTTCGTA (SEQ ID NO: 724)
310	HOMEOBOX PROTEIN GSH-2 (SEQ ID NO: 34)	TTTGTTGGTTTGTAGGA (SEQ ID NO: 725)
311	HOMEOBOX PROTEIN GSH-2 (SEQ ID NO: 34)	AGGACGGCGTTTATTA (SEQ ID NO: 726)
312	HOMEOBOX PROTEIN GSH-2 (SEQ ID NO: 34)	GATGAGGATGGTGTTT (SEQ ID NO: 727)
313	HOMEOBOX PROTEIN GSH-2 (SEQ ID NO: 34)	TTCGATTTCGGAGGAT (SEQ ID NO: 728)
314	HOMEOBOX PROTEIN GSH-2 (SEQ ID NO: 34)	TTTGATTTTGGAGGATT (SEQ ID NO: 729)
315	(SEQ ID NO: 35)	TTCGTTATCGAGAGTT (SEQ ID NO: 730)
316	(SEQ ID NO: 35)	GGGTTTTGTTATTGAGA (SEQ ID NO: 731)
317	(SEQ ID NO: 35)	GACGTGAGCGTTTAGG (SEQ ID NO: 732)

No:	Gene	Oligo:
318	(SEQ ID NO: 35)	GATGTGAGTGTTTAGGG (SEQ ID NO: 733)
319	(SEQ ID NO: 35)	TACGGAGTTGGCGTTA (SEQ ID NO: 734)
320	(SEQ ID NO: 35)	TTTATGGAGTTGGTGT (SEQ ID NO: 735)
321	(SEQ ID NO: 35)	TTGGTTCGTCGAGGAT (SEQ ID NO: 736)
322	(SEQ ID NO: 35)	TTGGTTTGTTGAGGAT (SEQ ID NO: 737)
323	HISTONE H4 (SEQ ID NO: 36)	ATCGAAATCGTAGAGG (SEQ ID NO: 738)
324	HISTONE H4 (SEQ ID NO: 36)	ATTGAAATTGTAGAGGG (SEQ ID NO: 739)
325	HISTONE H4 (SEQ ID NO: 36)	TATGGCGGTGATCGTT (SEQ ID NO: 740)
326	HISTONE H4 (SEQ ID NO: 36)	TTTATGGTGGTGATTGT (SEQ ID NO: 741)
327	HISTONE H4 (SEQ ID NO: 36)	TTACGGCGTTTCGGAT (SEQ ID NO: 742)
328	HISTONE H4 (SEQ ID NO: 36)	TTATGGTGTTTTGGATT (SEQ ID NO: 743)
329	HISTONE H4 (SEQ ID NO: 36)	ATGCGTTTTACGTCGT (SEQ ID NO: 744)
330	HISTONE H4 (SEQ ID NO: 36)	AGATGTGTTTTATGTTGT (SEQ ID NO: 745)
331	HISTONE H4 (SEQ ID NO: 36)	TAAGGCGTCGGATGGT (SEQ ID NO: 746)
332	HISTONE H4 (SEQ ID NO: 36)	GAGTAAGGTGTTGGAT (SEQ ID NO: 747)
333	HISTONE H4 (SEQ ID NO: 36)	TATTTTACGGTGGCGT (SEQ ID NO: 748)
334	HISTONE H4 (SEQ ID NO: 36)	ATTTTATGGTGGTGTTT (SEQ ID NO: 749)
335	POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2) (SEQ ID NO: 37)	ATTTCGGAGGTATCGT (SEQ ID NO: 750)
336	POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2	TTTGGAGGTATTGTGT (SEQ ID NO: 751)

No:	Gene	Oligo:
	(NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2) (SEQ ID NO: 37)	
337	POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2) (SEQ ID NO: 37)	TTCGTACGGGGTATAG (SEQ ID NO: 752)
338	POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2) (SEQ ID NO: 37)	GGTTTGTATGGGGTATA (SEQ ID NO: 753)
339	POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2) (SEQ ID NO: 37)	TATAAGGCGTTACGGT (SEQ ID NO: 754)
340	POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2) (SEQ ID NO: 37)	GGTATAAGGTGTTATGG (SEQ ID NO: 755)

No:	Gene	Oligo:
341	POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2) (SEQ ID NO: 37)	TTACGGTCGCGTAGTA (SEQ ID NO: 756)
342	POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2) (SEQ ID NO: 37)	TATGGTTGTGTAGTAGT (SEQ ID NO: 757)
343	ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22) (SEQ ID NO: 38)	TTATTCGTAGTTTTCGG (SEQ ID NO: 758)
344	ADAPTER-	GTTTATTTGTAGTTTTTGG

No:	Gene	Oligo:
	RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22) (SEQ ID NO: 38)	(SEQ ID NO: 759)
345	ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1	TGTAATCGTTTATTCGT (SEQ ID NO: 760)

No:	Gene	Oligo:
	CLATHRIN) (DC22) (SEQ ID NO: 38)	
346	ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22) (SEQ ID NO: 38)	TAATTGTTTATTTGTAGTTT (SEQ ID NO: 761)
347	ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1	TTCGAAGTCGGGATTA (SEQ ID NO: 762)

No:	Gene	Oligo:
	SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22) (SEQ ID NO: 38)	
348	ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22) (SEQ ID NO: 38)	ATTTTGAAGTTGGGATT (SEQ ID NO: 763)
349	ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT)	ATCGAGAGTATTTCGAAG (SEQ ID NO: 764)

No:	Gene	Oligo:
	(CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22) (SEQ ID NO: 38)	
350	ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22) (SEQ ID NO: 38)	GGATTGAGAGTATTTTGA (SEQ ID NO: 765)
351	(SEQ ID NO: 39)	TAAGCGGTATAAGTCGG (SEQ ID NO: 766)
352	(SEQ ID NO: 39)	AGTGGTATAAGTTGGTT (SEQ ID NO: 767)
353	(SEQ ID NO: 39)	TTCGGTAAGCGGTATA (SEQ ID NO: 768)
354	(SEQ ID NO: 39)	ATAATTTGGTAAGTGGTA (SEQ ID NO: 769)
355	(SEQ ID NO: 39)	TTCGTGATTTTACGTTA (SEQ ID NO: 770)
356	(SEQ ID NO: 39)	AATTTTGTGATTTTATGTT (SEQ ID NO: 771)

No:	Gene	Oligo:
357	(SEQ ID NO: 39)	TGGCGACGAAGTGTAA (SEQ ID NO: 772)
358	(SEQ ID NO: 39)	TTTGTGGTGATGAAGT (SEQ ID NO: 773)
359	(SEQ ID NO: 40)	TAGCGGGTTTACGGAG (SEQ ID NO: 774)
360	(SEQ ID NO: 40)	AGTAGTGGGTTTATGG (SEQ ID NO: 775)
361	(SEQ ID NO: 40)	TAACGAGTCGAGCGGA (SEQ ID NO: 776)
362	(SEQ ID NO: 40)	AATGAGTTGAGTGGAG (SEQ ID NO: 777)
363	(SEQ ID NO: 40)	TTTTCGCGTGTAAGTT (SEQ ID NO: 778)
364	(SEQ ID NO: 40)	TTTTTGTGTGTAAGTTAA (SEQ ID NO: 779)
365	(SEQ ID NO: 40)	TAGGACGATTCGGATA (SEQ ID NO: 780)
366	(SEQ ID NO: 40)	AGGATGATTTGGATAGT (SEQ ID NO: 781)
367	(SEQ ID NO: 40)	TTCGAGTGAAAGCGGTA (SEQ ID NO: 782)
368	(SEQ ID NO: 40)	TTTGAGTGAAAGTGGTA (SEQ ID NO: 783)
369	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	TTACGTTTTCGTGAAAT (SEQ ID NO: 784)
370	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	TTTTATGTTTTTGTGAAAT (SEQ ID NO: 785)
371	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)	GGGAGGACGTAGAGTA (SEQ ID NO: 786)

No:	Gene	Oligo:
	(SEQ ID NO: 41)	
372	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	GGGAGGATGTAGAGTA (SEQ ID NO: 787)
373	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	TGGGTTATCGTTTATATT (SEQ ID NO: 788)
374	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	TTGGGTTATTGTTTATATT (SEQ ID NO: 789)
375	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	TGGTATCGGTTTTTGAA (SEQ ID NO: 790)
376	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	TGGTATTGGTTTTTGAA (SEQ ID NO: 791)
377	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190	GTTTAGGTTCGAGTTTA (SEQ ID NO: 792)

No:	Gene	Oligo:
	KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	
378	PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN) (SEQ ID NO: 41)	GGTTTAGGTTTGAGTTTA (SEQ ID NO: 793)
379	(SEQ ID NO: 42)	AGAATTGCGACGGTTT (SEQ ID NO: 794)
380	(SEQ ID NO: 42)	AATTGTGATGGTTTGTA (SEQ ID NO: 795)
381	(SEQ ID NO: 42)	TTACGTTTATTTACGGG (SEQ ID NO: 796)
382	(SEQ ID NO: 42)	TATGTTTATTTATGGGGAT (SEQ ID NO: 797)
383	(SEQ ID NO: 42)	TGGATGTGCGGAAGAA (SEQ ID NO: 798)
384	(SEQ ID NO: 42)	GATGTGTGGAAGAAGT (SEQ ID NO: 799)
385	(SEQ ID NO: 42)	ATGGGTACGTTGTTTA (SEQ ID NO: 800)
386	(SEQ ID NO: 42)	TATGGGTATGTTGTTTAT (SEQ ID NO: 801)
387	(SEQ ID NO: 42)	GGATATTTGCGTTAGTA (SEQ ID NO: 802)
388	(SEQ ID NO: 42)	GGATATTTGTGTTAGTATT (SEQ ID NO: 803)
389	(SEQ ID NO: 43)	GACGTGTTCGGGTTTTA (SEQ ID NO: 804)
390	(SEQ ID NO: 43)	GATGTGTTTGGGTTTTA (SEQ ID NO: 805)
391	(SEQ ID NO: 43)	AGTCGACGGTTTGAGG (SEQ ID NO: 806)
392	(SEQ ID NO: 43)	AGTTGATGGTTTGAGG (SEQ ID NO: 807)
393	(SEQ ID NO: 43)	TTATTGCGTTGTTAAGT (SEQ ID NO: 808)
394	(SEQ ID NO: 43)	GTTATTGTGTTGTTAAGT (SEQ ID NO: 809)
395	(SEQ ID NO: 44)	ATTTAAACGGGGTCGT (SEQ ID NO: 810)
396	(SEQ ID NO: 44)	AATTTAAATGGGGTTGT (SEQ ID NO: 811)

No:	Gene	Oligo:
397	(SEQ ID NO: 44)	ATCGGTTTTTTGTATCGAATA (SEQ ID NO: 812)
398	(SEQ ID NO: 44)	ATTGGTTTTTTGTATTGAATA (SEQ ID NO: 813)
399	(SEQ ID NO: 44)	TTCGGCGTTTTCGTAG (SEQ ID NO: 814)
400	(SEQ ID NO: 44)	TGAAAGTTCGGCGTTT (SEQ ID NO: 815)
401	(SEQ ID NO: 44)	TTTGGTGTTTTTGTAGG (SEQ ID NO: 816)
402	(SEQ ID NO: 44)	TGAAAGTTTGGTGTTTT (SEQ ID NO: 817)
403	(SEQ ID NO: 45)	ATCGGTTTTTCGAGGT (SEQ ID NO: 818)
404	(SEQ ID NO: 45)	ATTGGTTTTTTGAGGTT (SEQ ID NO: 819)
405	(SEQ ID NO: 45)	GGTCGATTTTCGCGTA (SEQ ID NO: 820)
406	(SEQ ID NO: 45)	TGGTTGATTTTTGTGTA (SEQ ID NO: 821)
407	(SEQ ID NO: 46)	GGTAATTTCGCGTATT (SEQ ID NO: 822)
408	(SEQ ID NO: 46)	TTGGTAATTTTGTGTATTT (SEQ ID NO: 823)
409	(SEQ ID NO: 47)	TATGCGTATACGTGGT (SEQ ID NO: 824)
410	(SEQ ID NO: 47)	ATGTGTATATGTGGTTTT (SEQ ID NO: 825)
411	(SEQ ID NO: 47)	GTCGTTTTATGCGTAT (SEQ ID NO: 826)
412	(SEQ ID NO: 47)	TGGTTGTTTTATGTGTAT (SEQ ID NO: 827)
413	(SEQ ID NO: 47)	TAGTTTTCGAATTTCGT (SEQ ID NO: 828)
414	(SEQ ID NO: 47)	ATTAGTTTTTGAATTTTGT (SEQ ID NO: 829)
415	(SEQ ID NO: 48)	TAGCGAGGGTCGTTTT (SEQ ID NO: 830)
416	(SEQ ID NO: 48)	TAGTGAGGGTTGTTTT (SEQ ID NO: 831)
417	(SEQ ID NO: 48)	TTAGGTCGCGTCGGTA (SEQ ID NO: 832)
418	(SEQ ID NO: 48)	AGGTTGTGTTGGTAGA (SEQ ID NO: 833)
419	(SEQ ID NO: 48)	ATTTCGTTTACGTCGT (SEQ ID NO: 834)
420	(SEQ ID NO: 48)	GGATTTTGTTTATGTTGT (SEQ ID NO: 835)
421	(SEQ ID NO: 48)	TTTTCGTATTCGGGTA (SEQ ID NO: 836)

No:	Gene	Oligo:
422	(SEQ ID NO: 48)	TTTGTATTTGGGTAAAAG (SEQ ID NO: 837)
423	(SEQ ID NO: 48)	AGGATCGGGATTCGTA (SEQ ID NO: 838)
424	(SEQ ID NO: 48)	AGGATTGGGATTTGTAG (SEQ ID NO: 839)
425	(SEQ ID NO: 48)	TTCGTTTAAGCGGGGT (SEQ ID NO: 840)
426	(SEQ ID NO: 48)	TTTGTTTAAGTGGGGT (SEQ ID NO: 841)
427	(SEQ ID NO: 49)	ATATTCGTGCGGTCGG (SEQ ID NO: 842)
428	(SEQ ID NO: 49)	ATATTTGTGTGGTTGGA (SEQ ID NO: 843)
429	(SEQ ID NO: 49)	TTAGGTCGTGGAATGT (SEQ ID NO: 844)
430	(SEQ ID NO: 49)	TTAGGTTGTGGAATGT (SEQ ID NO: 845)
431	(SEQ ID NO: 49)	AGGAATCGTGAGTAGG (SEQ ID NO: 846)
432	(SEQ ID NO: 49)	AGGAATTGTGAGTAGG (SEQ ID NO: 847)
433	DNA REPLICATION FACTOR; DOUBLE PARKED, DROSOPHILA, HOMOLOG OF (SEQ ID NO: 50)	TTCGATATCGAGTCGG (SEQ ID NO: 848)
434	DNA REPLICATION FACTOR; DOUBLE PARKED, DROSOPHILA, HOMOLOG OF (SEQ ID NO: 50)	ATTTGATATTGAGTTGGT (SEQ ID NO: 849)
435	DNA REPLICATION FACTOR; DOUBLE PARKED, DROSOPHILA, HOMOLOG OF (SEQ ID NO: 50)	ATTCGCGTTTTAACGT (SEQ ID NO: 850)
436	DNA REPLICATION FACTOR; DOUBLE	TTTGTGTTTTAATGTGGA (SEQ ID NO: 851)

No:	Gene	Oligo:
	PARKED, DROSOPHILA, HOMOLOG OF (SEQ ID NO: 50)	
437	DNA REPLICATION FACTOR; DOUBLE PARKED, DROSOPHILA, HOMOLOG OF (SEQ ID NO: 50)	TTCGGTTGGGACGTAA (SEQ ID NO: 852)
438	DNA REPLICATION FACTOR; DOUBLE PARKED, DROSOPHILA, HOMOLOG OF (SEQ ID NO: 50)	TTTGGTTGGGATGTAA (SEQ ID NO: 853)
439	DNA REPLICATION FACTOR; DOUBLE PARKED, DROSOPHILA, HOMOLOG OF (SEQ ID NO: 50)	TTAAGGCGTTTAGCGA (SEQ ID NO: 854)
440	DNA REPLICATION FACTOR; DOUBLE PARKED, DROSOPHILA, HOMOLOG OF (SEQ ID NO: 50)	TTTTAAGGTGTTTAGTGA (SEQ ID NO: 855)
441	PR-DOMAIN ZINC FINGER PROTEIN 16 (TRANSCRIPTION FACTOR MEL1) (SEQ ID NO: 51)	TATCGTCGAGTGTGTA (SEQ ID NO: 856)
442	PR-DOMAIN ZINC FINGER PROTEIN 16 (TRANSCRIPTION FACTOR MEL1) (SEQ ID NO: 51)	GGGGTTATTGTTGAGT (SEQ ID NO: 857)
443	PR-DOMAIN ZINC FINGER PROTEIN	TATTATTCGAGTTAGAGG (SEQ ID NO: 858)

No:	Gene	Oligo:
	16 (TRANSCRIPTION FACTOR MEL1) (SEQ ID NO: 51)	
444	PR-DOMAIN ZINC FINGER PROTEIN 16 (TRANSCRIPTION FACTOR MEL1) (SEQ ID NO: 51)	TTATTATTTGAGTTAGAGG (SEQ ID NO: 859)
445	PR-DOMAIN ZINC FINGER PROTEIN 16 (TRANSCRIPTION FACTOR MEL1) (SEQ ID NO: 51)	AGGATTCGTTGAAGAA (SEQ ID NO: 860)
446	PR-DOMAIN ZINC FINGER PROTEIN 16 (TRANSCRIPTION FACTOR MEL1) (SEQ ID NO: 51)	GTAGGATTTGTTGAAGA (SEQ ID NO: 861)
447	PR-DOMAIN ZINC FINGER PROTEIN 16 (TRANSCRIPTION FACTOR MEL1) (SEQ ID NO: 51)	TTATTAGGCGATATTTTAA (SEQ ID NO: 862)
448	PR-DOMAIN ZINC FINGER PROTEIN 16 (TRANSCRIPTION FACTOR MEL1) (SEQ ID NO: 51)	TATTAGGTGATATTTTAAGT (SEQ ID NO: 863)
449	TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-	TAGTACGTTGGTTCGG (SEQ ID NO: 864)

No:	Gene	Oligo:
	LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	
450	TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	TATGTTGGTTTGGAGT (SEQ ID NO: 865)
451	TUMOR SUPPRESSING	AGTTGTTCGATGATTAG (SEQ ID NO: 866)

No:	Gene	Oligo:
	SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	
452	TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-	TTTAGTTGTTTGATGATTA (SEQ ID NO: 867)

No:	Gene	Oligo:
	LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	
453	TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	AGATTAGTACGTTGGTT (SEQ ID NO: 868)
454	TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-	AAGATTAGTATGTTGGTT (SEQ ID NO: 869)

No:	Gene	Oligo:
	WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	
455	TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED	TTAAAGCGGGGAGTTT (SEQ ID NO: 870)

No:	Gene	Oligo:
	MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	
456	TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	GTTTAAAGTGGGGAGT (SEQ ID NO: 871)
457	TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN	AGATGGTATCGTTTAGG (SEQ ID NO: 872)

No:	Gene	Oligo:
	SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	
458	TUMOR SUPPRESSING SUBTRANSFERABLE CANDIDATE 5; P45 BECKWITH-WIEDEMANN REGION 1A; BECKWITH-WIEDEMANN SYNDROME CHROMOSOME REGION 1, CANDIDATE A; EFFLUX TRANSPORTER-LIKE PROTEIN; ORGANIC CATION TRANSPORTER-LIKE 2; TUMOR-SUPPRESSING STF CDNA 5; IMPRINTED MULTI-MEMBRANE SPANNING POLYSPECIFIC	ATGGTATTGTTTAGGTG (SEQ ID NO: 873)

No:	Gene	Oligo:
	TRANSPORTER-RELATED PROTEIN (SEQ ID NO: 52)	
459	CDH1 (SEQ ID NO: 54)	TATCGCGTTTATGCGA (SEQ ID NO: 874)
460	CDH1 (SEQ ID NO: 54)	ATTGTGTTTATGTGAGG (SEQ ID NO: 875)
461	CDH1 (SEQ ID NO: 54)	TTATGCGAGGTCGGGT (SEQ ID NO: 876)
462	CDH1 (SEQ ID NO: 54)	TTATGTGAGGTTGGGT (SEQ ID NO: 877)
463	CDH1 (SEQ ID NO: 54)	TTAATTAGCGGTACGG (SEQ ID NO: 878)
464	CDH1 (SEQ ID NO: 54)	AATTAGTGGTATGGGG (SEQ ID NO: 879)
465	CDH1 (SEQ ID NO: 54)	TAGTGGCGTCGGAATT (SEQ ID NO: 880)
466	CDH1 (SEQ ID NO: 54)	TAGTGGTGTTGGAATT (SEQ ID NO: 881)
467	CDKN2a (SEQ ID NO: 55)	GGCGTTGTTTAACGTAT (SEQ ID NO: 882)
468	CDKN2a (SEQ ID NO: 55)	GGGTGTTGTTTAATGTA (SEQ ID NO: 883)
469	CDKN2a (SEQ ID NO: 55)	TGTTTAACGTATCGAAT (SEQ ID NO: 884)
470	CDKN2a (SEQ ID NO: 55)	GTTGTTTAATGTATTGAAT (SEQ ID NO: 885)
471	CDKN2a (SEQ ID NO: 55)	AATAGTTACGGTCGGA (SEQ ID NO: 886)
472	CDKN2a (SEQ ID NO: 55)	AGTTATGGTTGGAGGT (SEQ ID NO: 887)
473	CDKN2a (SEQ ID NO: 55)	GTCGGAGGTCGATTTA (SEQ ID NO: 888)
474	CDKN2a (SEQ ID NO: 55)	GGTTGGAGGTTGATTTA (SEQ ID NO: 889)
475	CD44 (SEQ ID NO: 56)	AGGTATTTCGCGATAT (SEQ ID NO: 890)
476	CD44 (SEQ ID NO: 56)	AGGTATTTTGTGATATTTT (SEQ ID NO: 891)
477	CD44 (SEQ ID NO: 56)	TAGGTTCGGTTCGTTAT (SEQ ID NO: 892)
478	CD44 (SEQ ID NO: 56)	TAGGTTTGGTTTGTTATT (SEQ ID NO: 893)
479	CD44 (SEQ ID NO: 56)	GTTCGTTTCGGATATTA (SEQ ID NO: 894)
480	CD44 (SEQ ID NO: 56)	TTTGTTTTGGATATTATGG (SEQ ID NO: 895)
481	CD44 (SEQ ID NO: 56)	TTTGGCGTAGATCGGT (SEQ ID NO: 896)

No:	Gene	Oligo:
482	CD44 (SEQ ID NO: 56)	TTTGGTGTAGATTGGT (SEQ ID NO: 897)
483	CD44 (SEQ ID NO: 56)	TTTAGCGCGGATTCGG (SEQ ID NO: 898)
484	CD44 (SEQ ID NO: 56)	GTTTAGTGTGGATTTGG (SEQ ID NO: 899)
485	GSTP1 (SEQ ID NO: 57)	ATCGTTGCGATTTCGG (SEQ ID NO: 900)
486	GSTP1 (SEQ ID NO: 57)	ATTGTTGTGATTTTGGA (SEQ ID NO: 901)
487	GSTP1 (SEQ ID NO: 57)	AGTGTGCGTAGCGAAT (SEQ ID NO: 902)
488	GSTP1 (SEQ ID NO: 57)	GTGTGTAGTGAATTGG (SEQ ID NO: 903)
489	GSTP1 (SEQ ID NO: 57)	GAGTCGTCGCGTAGTT (SEQ ID NO: 904)
490	GSTP1 (SEQ ID NO: 57)	GGAGTTGTTGTGTAGTT (SEQ ID NO: 905)
491	GSTP1 (SEQ ID NO: 57)	ATTTTCGTCGGTTTTAG (SEQ ID NO: 906)
492	GSTP1 (SEQ ID NO: 57)	GGATTTTTGTTGGTTTTA (SEQ ID NO: 907)
493	GSTP1 (SEQ ID NO: 57)	TTCGCGGTTTTCGAGT (SEQ ID NO: 908)
494	GSTP1 (SEQ ID NO: 57)	TTTGTGGTTTTTGAGTT (SEQ ID NO: 909)
495	GSTP1 (SEQ ID NO: 57)	TAGCGAAGTTTCGCGG (SEQ ID NO: 910)
496	GSTP1 (SEQ ID NO: 57)	AGTGAAGTTTTGTGGT (SEQ ID NO: 911)
497	GSTP1 (SEQ ID NO: 57)	GTCGCGCGTATTTATT (SEQ ID NO: 912)
498	GSTP1 (SEQ ID NO: 57)	GGGTTGTGTGTATTTAT (SEQ ID NO: 913)
499	IGF2 (SEQ ID NO: 58)	TACGTATAAAATTTCGTATT (SEQ ID NO: 914)
500	IGF2 (SEQ ID NO: 58)	AAATTATGTATAAAATTTTGT (SEQ ID NO: 915)
501	IGF2 (SEQ ID NO: 58)	ATAGACGCGAGTTCGG (SEQ ID NO: 916)
502	IGF2 (SEQ ID NO: 58)	AGATGTGAGTTTGGTT (SEQ ID NO: 917)
503	IGF2 (SEQ ID NO: 58)	TATCGGGGTGCGTTTA (SEQ ID NO: 918)
504	IGF2 (SEQ ID NO: 58)	ATTGGGGTGTGTTTAA (SEQ ID NO: 919)
505	IGF2 (SEQ ID NO: 58)	TTACGGAGGTTTCGGT (SEQ ID NO: 920)
506	IGF2 (SEQ ID NO: 58)	TTATGGAGGTTTTGGT (SEQ ID NO: 921)

No:	*Gene*	*Oligo:*
507	AR (SEQ ID NO: 53)	TTATAGTCGTAGTCGGT (SEQ ID NO: 922)
508	AR (SEQ ID NO: 53)	AGTTGTAGTTGGTTTTG (SEQ ID NO: 923)
509	AR (SEQ ID NO: 53)	GTCGTGGTCGTTAGTA (SEQ ID NO: 924)
510	AR (SEQ ID NO: 53)	GTTGTGGTTGTTAGTAA (SEQ ID NO: 925)
511	AR (SEQ ID NO: 53)	TATTTTCGGACGAGGA (SEQ ID NO: 926)
512	AR (SEQ ID NO: 53)	AGTATTTTTGGATGAGG (SEQ ID NO: 927)

Example 4:

In the following analysis the methylation status of the genes according to Table 10 were analysed by means of methylation specific polymerase chain reaction using the primers according to Table 10 (below).

The study was run on 50 prostate cancer and 50 Benign Prostate Hyperplasia (BPH) tissue samples. Genomic DNA was analyzed using the MSP technique after bisulfite conversion. The bisulfite process converts unmethylated cytosines to uracil while methylated cytosines remained conserved. Bisulfite treatment was performed with minor modifications according to the protocol described in Olek et al. (1996). Sequences of interest were then amplified by means of methylation specific primers, and the amplificate is detected by means of Taqman probes (see Table 10).

Table 10

Genomic SEQ ID NO:	Primer	Primer	Taqman probe
20	Cgcgctactccgcataca (SEQ ID NO: 958)	Gaggtaatcgaggcggtcg (SEQ ID NO: 959)	56-FAM/cgccaattcatacgccgcacc/3BHQ (SEQ ID NO: 960)
36	Accgaaaatacgcttcacg (SEQ ID NO: 961)	Gcgttatcgtaaagtattgcgc (SEQ ID NO: 962)	/56-FAM/cgcgacgaacaaaacgccg/3BHQ_1/ (SEQ ID NO: 963)
36	Gcgttttacgtcgtcgcg (SEQ ID NO: 964)	Gacgctaaacgccaccgt (SEQ ID NO: 965)	/56-FAM/ccgaccatccgacgccttactcg/3BHQ_1/ (SEQ ID NO: 966)
51	Cgaatttataccgaacgctcctacg (SEQ ID NO: 967)	Aggttacgggaggtcgaggtcg (SEQ ID NO: 968)	56-FAM/ cccgccatcgaccgttcccgaccccta/3BHQ (SEQ

			ID NO: 969)
51	Tcccgaatttataccgaacg (SEQ ID NO: 970)	Ttttatttaggggtcgggaac (SEQ ID NO: 971)	56-FAM/ acgccccgccatcgaccg/3BHQ_1 (SEQ ID NO: 972)
24	Ttgtggttcgggaagagac (SEQ ID NO: 973)	Cttcgatcgaaaaaaaccg (SEQ ID NO: 974)	56-FAM/ aactacgcgcaaacccgcga/3BHQ (SEQ ID NO: 975)
31	Cgtttttcgttttattttcgc (SEQ ID NO: 976)	Gacaaaaaacgccacgtc (SEQ ID NO: 977)	56-FAM/ccgacaattcaccgaatcaccg/3BHQ_1 (SEQ ID NO: 978)
11	Atctcacctaccgtcgcg (SEQ ID NO: 979)	Taggagtgcgatcgtttgc (SEQ ID NO: 980)	56-FAM/acgaacgttacgaccgatacccaacta/3BHQ (SEQ ID NO: 981)
4	Aacgtatcccgacaatccg (SEQ ID NO: 982)	Gagtatttaaggtttagtgaaacgttagc (SEQ ID NO: 983)	56-FAM/ caaataacgcgacactaaacgcataattc/3BHQ_1 (SEQ ID NO: 984)
4	Tgttttcggagtgcgttc (SEQ ID NO: 985)	Aaatcaaaccgacgatacga (SEQ ID NO: 986)	56-FAM/ ccgataaaacgcgtccaaaccg/3BHQ (SEQ ID NO: 987)

Reagents:

A standard set of reagent and cycling conditions are used for MSP establishment and template amplification. Standard conditions are outlined in tables X & Y. Prior to running biological samples, amplicons were established using 100 picograms of completely methylated DNA as a positive control and and 100 nanograms of unmethylated DNA as a negative control. Reaction conditions were also checked for relative sensitivity using 50 picograms of methylated DNA in a background of 50 nanograms of unmethylated DNA. Reagent concentrations are outlined in Table 11 and cycling conditions for the ABI 7700 are defined in Table 12.

Table 11

Reagent	Stock Conc. (uM)	Final Rx Conc. (nM)	MM Conc. (uM)	MM Volume (uL)
Forward	10.0	500.0	3.33	35.0
Reverse	10.0	500.0	3.33	35.0
Probe	100.0	400.0	2.67	2.8
Water	-	-	-	32.2
Taqmix	-	-	-	245.0
Total	-	-	-	350.0

Cycling conditions

Table 12

Temperature (C)	Time (sec)	# of Cycles
Denature		1
95	600	
Annealing		50
95	10	
60 or 63	45	

Data analysis

Class prediction by supervised learning

In order to give a reliable estimate of how well the CpG ensemble of a selected marker can differentiate between different tissue classes we can determine its prediction accuracy by classification. For that purpose we calculate a methylation profile-based prediction function using a certain set of tissue samples with a specific class label. This step is called training and it exploits the prior knowledge represented by the data labels. The prediction accuracy of that function is then tested on a set of independent samples. As a method of choice, we use the support vector machine (SVM) algorithm (see e.g. Cristiannini, N. and Shawe-Taylor, J. An introduction to support vector machines. Cambridge, UK: Cambridge University Press, 2000.; Duda, R. O., Hart, P. E., and Stork, D. G. Pattern Classification. New York: John Wiley & Sons, 2001.) to learn the prediction function. For this report, sensitivity and specificity are weighted equally. This is achieved by setting the risk associated with false positive and false negative classifications to be inversely proportional to the respective class sizes. Therefore sensitivity and specificity of the resulting classifier can be expected to be approximately equal. Note that this weighting can be adapted according to the clinical requirements.

Results

To determine sensitivity and specificity of said markers, 50 prostate cancer and 50 BPH samples were screened using the defined parameters. Samples had been pre-screened following a technical criterion of methylated DNA vs. unmethylated DNA. After ensuring they were specific for methylated DNA while not amplifying common unmethylated DNA, assays were run using MethyLight realtime PCR on a TaqMan platform (ABI7900). Final assay performance is outlined in Table 13. AUC and corresponding sensitivity and specificity values were calculated using the SVM algorithms.

Results: Table 13

Gene name	Genomic SEQ ID NO:	AUC	Sensitivity	Specificity
PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE	20	0,921	0,829	0,871
HISTONE H4	36	0,918	0,88	0,719
PR-DOMAIN ZINC FINGER PROTEIN 16	51	0,871	0,768	0,822
ORPHAN NUCLEAR RECEPTOR NR5A2	24	0,859	0,694	0,878
LIM DOMAIN KINASE 1	31	0,868	0,791	0,755
Genomic region	11	0,842	0,815	0,704
LIM/HOMEOBOX PROTEIN LHX9	4	0,745	0,695	0,653

We claim:

1. A method for detecting and/or distinguishing between or among prostate cell proliferative disorders in a subject, said method comprising analysing the methylation pattern of a target nucleic acid comprising one or a combination of sequences taken from the group consisting of SEQ ID NO: 1 to SEQ ID NO:59 by contacting at least one of said target nucleic acids in a biological sample obtained from said subject with at least one reagent, or series of reagents that distinguishes between methylated and non-methylated CpG dinucleotides.

2. The method of claim 1, wherein prostate cancer is distinguished from at least one condition selected from the group consisting of one of normal prostate and/or benign prostate hyperplasia.

3. The method of claim 2 wherein said target sequences are of the genomic sequences as shown in Table 4.

4. The method of claim 1, wherein prostate cancer is distinguished from at least one condition selected from the group consisting of normal prostate, normal tissue from other tissues, cancer of other tissues and/or benign prostate hyperplasia.

5. The method of claim 2 wherein said target sequences are of the genomic sequences as shown in Table 5.

6. The method of claim 1, wherein prostate cancer is distinguished from cancers of other tissues.

7. The method of claim 2 wherein said target sequences are of the genomic sequences as shown in Table 6.

8. A method for detecting and/or distinguishing between or among prostate cell proliferative disorders in a subject, comprising:
-obtaining, from a subject, a biological sample having subject genomic DNA;
-contacting the genomic DNA, or a fragment thereof, with one reagent or a plurality of reagents for distinguishing between methylated and non methylated CpG dinucleotide sequences within at least one target sequence of the genomic DNA, or fragment thereof, wherein the target sequence comprises, or hybridizes under stringent

conditions to, at least 16 contiguous nucleotides of a sequence taken from the group consisting of SEQ ID NO: 1 to SEQ ID NO 59, said contiguous nucleotides comprising at least one CpG dinucleotide sequence; and

-determining, based at least in part on said distinguishing, the methylation state of at least one target CpG dinucleotide sequence, or an average, or a value reflecting an average methylation state of a plurality of target CpG dinucleotide sequences, whereby detecting, or detecting and distinguishing between or among prostate cell proliferative disorders is, at least in part, afforded.

9. The method of claim 8, wherein distinguishing between methylated and non methylated CpG dinucleotide sequences within the target sequence comprises converting unmethylated cytosine bases within the target sequence to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties.

10. The method of claim 8, wherein distinguishing between methylated and non methylated CpG dinucleotide sequences within the target sequence(s) comprises methylation state-dependent conversion or non-conversion of at least one CpG dinucleotide sequence to the corresponding converted or non-converted dinucleotide sequence within a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and contiguous regions thereof corresponding to the target sequence.

11. The method of claim 8, wherein the biological sample is selected from the group consisting of cell lines, histological slides, biopsies, paraffin-embedded tissue, bodily fluids, ejaculate, urine, blood, and combinations thereof.

12. The method of claim 8, wherein distinguishing between methylated and non methylated CpG dinucleotide sequences within the target sequence comprises use of at least one nucleic acid molecule or peptide nucleic acid (PNA) molecule comprising, in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof.

13. The method of claim 12, wherein the contiguous sequence comprises at least one CpG, TpG or CpA dinucleotide sequence.

14. The method of claim 12, comprising use of at least two such nucleic acid molecules, or peptide nucleic acid (PNA) molecules.

15. The method of claim 12, comprising use of at least two such nucleic acid molecules, or peptide nucleic acid (PNA) molecules as primer oligonucleotides for the amplification of a sequences selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, sequences complementary thereto, and regions thereof that comprise, or hybridize under stringent conditions to the primers.

16. The method of claim 14, comprising use of at least four such nucleic acid molecules, or peptide nucleic acid (PNA) molecules.

17. A method for detecting, or detecting and distinguishing between or among prostate cell proliferative disorders in a subject, comprising:

   a. obtaining, from a subject, a biological sample having subject genomic DNA;
   b. extracting or otherwise isolating the genomic DNA;
   c. treating the genomic DNA of b), or a fragment thereof, with one or more reagents to convert cytosine bases that are unmethylated in the 5-position thereof to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties;
   d. contacting the treated genomic DNA, or the treated fragment thereof, with an amplification enzyme and at least two primers comprising, in each case a contiguous sequence of at least 9 nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof, wherein the treated genomic DNA or the fragment thereof is either amplified to produce at least one amplificate, or is not amplified; and

   e. determining, based on a presence or absence of, or on a property of said amplificate, the methylation state of at least one CpG dinucleotide of a sequence selected from the group consisting SEQ ID NO: 1 to SEQ ID NO 59, or an average, or a value reflecting an average methylation state of a plurality

of CpG dinucleotides of a sequence selected from the groups consisting of SEQ ID NO: 1 to SEQ ID NO 59, whereby at least one of detecting, or detecting and distinguishing between prostate cell proliferative disorders is, at least in part, afforded.

18. The method of claim 17, wherein treating the genomic DNA, or the fragment thereof in c), comprises use of a reagent selected from the group consisting of bisulfite, hydrogen sulfite, disulfite, and combinations thereof.

19. The method of claim 17, wherein contacting or amplifying in d) comprises use of at least one method selected from the group consisting of: use of a heat-resistant DNA polymerase as the amplification enzyme; use of a polymerase lacking 5'-3' exonuclease activity; use of a polymerase chain reaction (PCR); generation of a amplificate nucleic acid molecule carrying a detectable labels; and combinations thereof.

20. The method of claim 19, wherein the detectable amplificate label is selected from the label group consisting of: fluorescent labels; radionuclides or radiolabels; amplificate mass labels detectable in a mass spectrometer; detachable amplificate fragment mass labels detectable in a mass spectrometer; amplificate, and detachable amplificate fragment mass labels having a single-positive or single-negative net charge detectable in a mass spectrometer; and combinations thereof.

21. The method of claim 17, wherein the biological sample obtained from the subject is selected from the group consisting of cell lines, histological slides, biopsies, paraffin-embedded tissue, bodily fluids, ejaculate, urine, blood, and combinations thereof.

22. The method of claim 17, wherein prostate cancer is distinguished from at least one condition selected form the group consisting of prostate adenoma, inflammatory prostate tissue, prostate adenomas with grade 2 dysplasia less than 1 cm, prostate adenomas with grade 3 dysplasia equal to or greater than 1 cm in size, normal prostate tissues, non-prostate normal tissue, body fluids, and non-prostate cancer tissue. The method of claim 12, further comprising in step d) the use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group

consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which it is hybridized.

23. The method of claim 22, wherein said nucleic acid molecule or peptide nucleic acid molecule is in each case modified at the 5'-end thereof to preclude degradation by an enzyme having 5'-3' exonuclease activity.

24. The method of claim 22, wherein said nucleic acid molecule or peptide nucleic acid molecule is in each case lacking a 3' hydroxyl group.

25. The method of claim 22, wherein the amplification enzyme is a polymerase lacking 5'-3' exonuclease activity.

26. The method of claim 17, wherein determining in e) comprises hybridization of at least one nucleic acid molecule or peptide nucleic acid molecule in each case comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof.

27. The method of claim 26, wherein at least one such hybridizing nucleic acid molecule or peptide nucleic acid molecule is bound to a solid phase.

28. The method of claim 26, wherein a plurality of such hybridizing nucleic acid molecules or peptide nucleic acid molecules are bound to a solid phase in the form of a nucleic acid or peptide nucleic acid array selected from the array group consisting of linear or substantially so, hexagonal or substantially so, rectangular or substantially so, and combinations thereof.

29. The method of claim 26, further comprising extending at least one such hybridized nucleic acid molecule by at least one nucleotide base.

30. The method of claim 17, wherein determining in e), comprises sequencing of the amplificate.

31. The method of claim 17, wherein contacting or amplifying in d), comprises use of methylation-specific primers.

32. The method of claim 17 comprising in d) using primer oligonucleotides comprising one or more CpG; TpG or CpA dinucleotides; and further comprising in e) the use of at least one method selected from the group consisting of: hybridizing in at least one nucleic acid molecule or peptide nucleid acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof; hybridizing at least one nucleic acid molecule that is bound to a solid phase and comprises a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof; hybridizing at least one nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof, and extending at least one such hybridized nucleic acid molecule by at least one nucleotide base; and sequencing in e) of the amplificate.

33. The method of claim 17 comprising in d) use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which it is hybridized; and further comprising in e) the use of at least one method selected from the group consisting of: hybridizing in at least one nucleic acid molecule or peptide nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof; hybridizing at least one nucleic acid molecule that is bound to a solid phase and comprises a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof; hybridizing at least one nucleic acid molecule comprising a contiguous sequence at

least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof, and extending at least one such hybridized nucleic acid molecule by at least one nucleotide base; and sequencing in e) of the amplificate.

34. The method of claim 17, comprising in d) amplification by primer oligonucleotides comprising one or more CpG; TpG or CpA dinucleotides and further comprising in e) hybridizing at least one detectably labeled nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295.

35. The method of claim 17, comprising in d) the use of at least one nucleic acid molecule or peptide nucleic acid molecule comprising in each case a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof, wherein said nucleic acid molecule or peptide nucleic acid molecule suppresses amplification of the nucleic acid to which it is hybridized, and further comprising in e) hybridizing at least one detectably labeled nucleic acid molecule comprising a contiguous sequence at least 9 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295.

36. A method for detecting and/or distinguishing between or among prostate cell proliferative disorders in a subject, comprising:

a. obtaining, from a subject, a biological sample having subject genomic DNA;
b. extracting, or otherwise isolating the genomic DNA;
c. contacting the genomic DNA of b), or a fragment thereof, comprising at least 16 contiguous nucleotides of a sequence selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO 59 and sequences that hybridize under stringent conditions thereto, with one or more methylation-sensitive restriction enzymes, wherein the genomic DNA is, with respect to each cleavage recognition motif

thereof, either cleaved thereby to produce cleavage fragments, or not cleaved thereby; and

d. determining, based on a presence or absence of, or on property of at least one such cleavage fragment, the methylation state of at least one CpG dinucleotide of a sequence selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO 59, or an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotides of a sequence selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO 59, whereby at least one of detecting, or of detecting and differentiating between or among prostate cell proliferative disorders is, at least in part, afforded.

37. The method of claim 36, further comprising, prior to determining in d), amplifying of the digested or undigested genomic DNA.

38. The method of claim 37, wherein amplifying comprises use of at least one method selected from the group consisting of: use of a heat resistant DNA polymerase as an amplification enzyme; use of a polymerase lacking 5'-3' exonuclease activity; use of a polymerase chain reaction (PCR); generation of a amplificate nucleic acid carrying a detectable label; and combinations thereof.

39. The method of claim 38, wherein the detectable amplificate label is selected from the label group consisting of: fluorescent labels; radionuclides or radiolabels; amplificate mass labels detectable in a mass spectrometer; detachable amplificate fragment mass labels detectable in a mass spectrometer; amplificate, and detachable amplificate fragment mass labels having a single-positive or single-negative net charge detectable in a mass spectrometer; and combinations thereof.

40. The method of claim 36, wherein the biological sample obtained from the subject is selected from the group consisting of cell lines, histological slides, biopsies, paraffin-embedded tissue, bodily fluids, ejaculate, urine, blood, and combinations thereof.

41. A treated nucleic acid derived from genomic SEQ ID NO: 1 to SEQ ID NO 59, wherein the treatment is suitable to convert at least one unmethylated cytosine base of

the genomic DNA sequence to uracil or another base that is detectably dissimilar to cytosine in terms of hybridization.

42. A nucleic acid, comprising at least 16 contiguous nucleotides of a treated genomic DNA sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and sequences complementary thereto, wherein the treatment is suitable to convert at least one unmethylated cytosine base of the genomic DNA sequence to uracil or another base that is detectably dissimilar to cytosine in terms of hybridization.

43. The nucleic acid of claims 41 and 42 wherein the contiguous base sequence comprises at least one CpG, TpG or CpA dinucleotide sequence.

44. The nucleic acid of claims 41 and 42 wherein the treatment comprises use of a reagent selected from the group consisting of bisulfite, hydrogen sulfite, disulfite, and combinations thereof.

45. An oligomer, comprising a sequence of at least 9 contiguous nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a treated genomic DNA sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295.

46. The oligomer of claim 45, comprising at least one CpG, CpA or TpG dinucleotide.

47. A set of oligomers, comprising at least two oligonucleotides according, in each case, to any one of Claims 45 or 46.

48. Use of a set of oligomers according, in each case, to any Claim 47, as probes for determining at least one of a cytosine methylation state, or a single nucleotide polymorphism (SNP) of a sequence selected from the group consisting of SEQ ID NO: 1 to 59 and sequences complementary thereto.

49. A method for manufacturing a nucleic acid array, comprising at least one of attachment of an oligomer according to any one of claims 45 or 46, or attachment of a set of oligomers or nucleic acids according to claim 47, to a solid phase.

50. An oligomer array manufactured according to claim 49.

51. The oligomer array of claim 50, wherein the oligomers are bound to a planar solid phase in the form of a lattice selected from the group consisting of linear or substantially linear lattice, hexagonal or substantially hexagonal lattice, rectangular or substantially rectangular lattice, and lattice combinations thereof

52. Use of the oligomer array of claim 50 for the analysis of prostate cell proliferative disorders.

53. The array of claim 50, wherein the solid phase surface comprises a material selected from the group consisting of silicon, glass, polystyrene, aluminium, steel, iron, copper, nickel, silver, gold, and combinations thereof.

54. A kit useful for detecting, or for detecting distinguishing between or among prostate cell proliferative disorders of a subject, comprising:

-at least one of a bisulfite reagent, or a methylation-sensitive restriction enzyme; and

-at least one nucleic acid molecule or peptide nucleic acid molecule comprising, in each case a contiguous sequence at least 9 nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NO: 60 to SEQ ID NO: 295, and complements thereof

55. The kit of claim 54, further comprising standard reagents for performing a methylation assay selected from the group consisting of MS-SNuPE, MSP, MethyLight, HeavyMethyl, nucleic acid sequencing, and combinations thereof.

56. Use of a method according to claims 1 to 41, a nucleic acid according to claims 41 through 44, an oligomer according to any one of claims 45 and 46, a set of oligonucleotides according to claim 47, an array according to any one of claim 50 through 53 and a kit according to claims 54 and 55 for the detection of and/or differentiation between or among subclasses of, prostate cell proliferative disorders.

Abstract

The invention provides methods, nucleic acids and kits for detecting and/or distinguishing between or among prostate cell proliferative disorders. The invention discloses genomic sequences the methylation patterns of which have utility for the improved detection of and differentiation between said class of disorders, thereby enabling the improved diagnosis and treatment of patients.

Figure 3

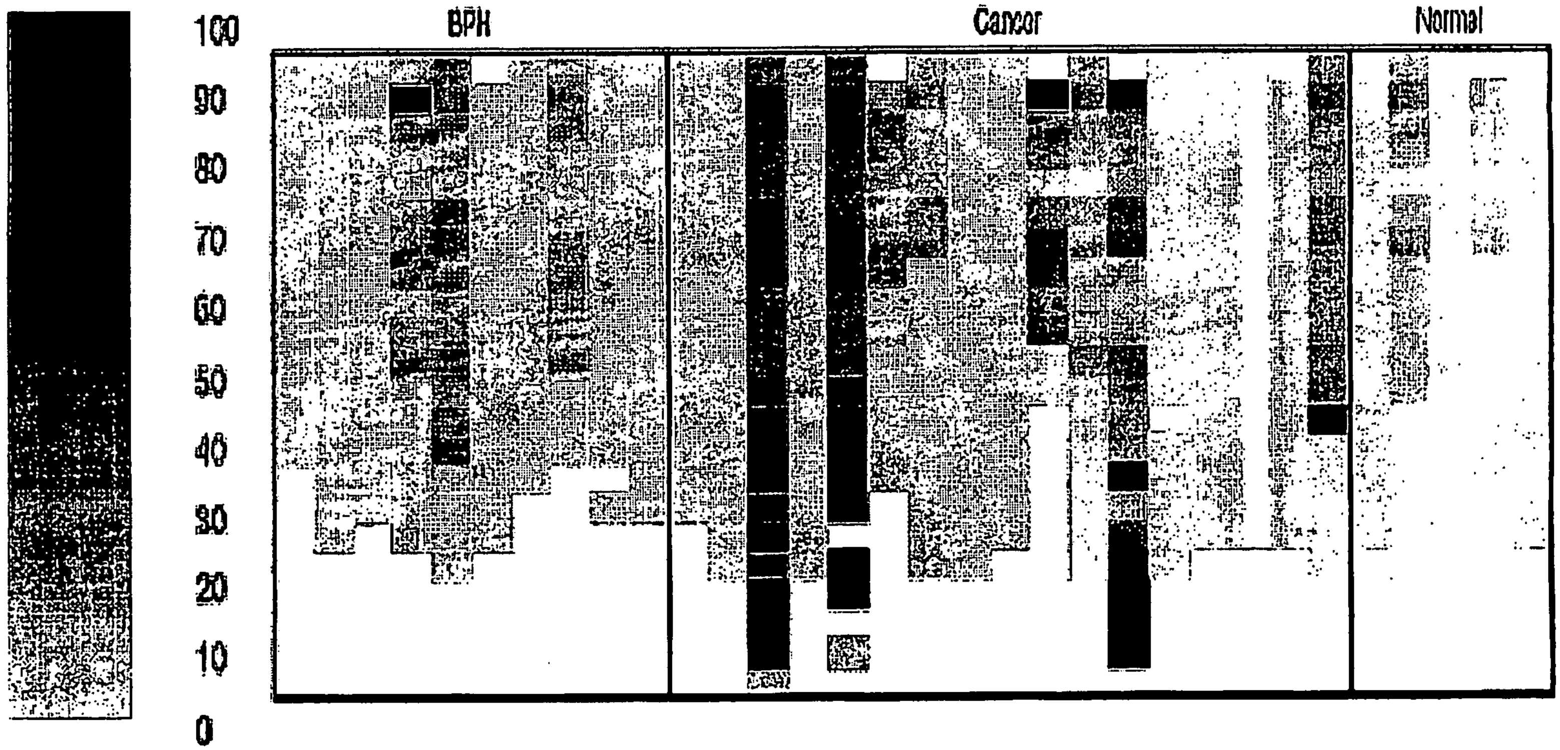
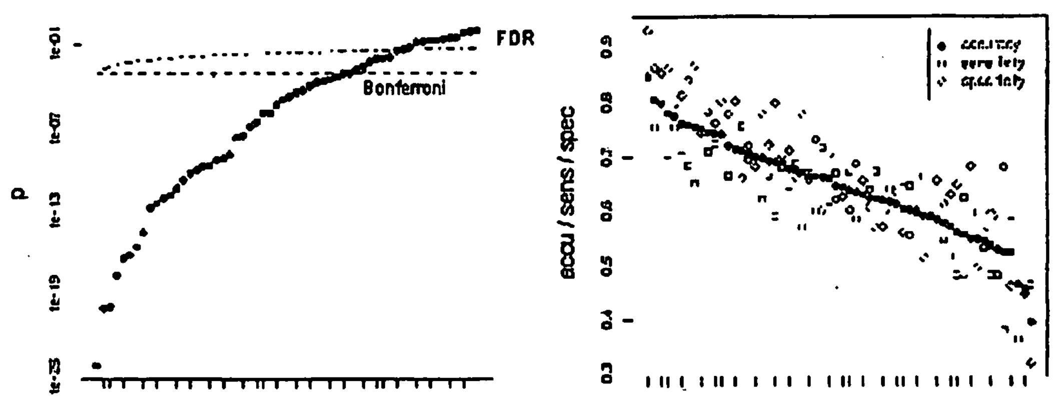


Figure 4



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FDR
Bonferroni
accu / sens / spec
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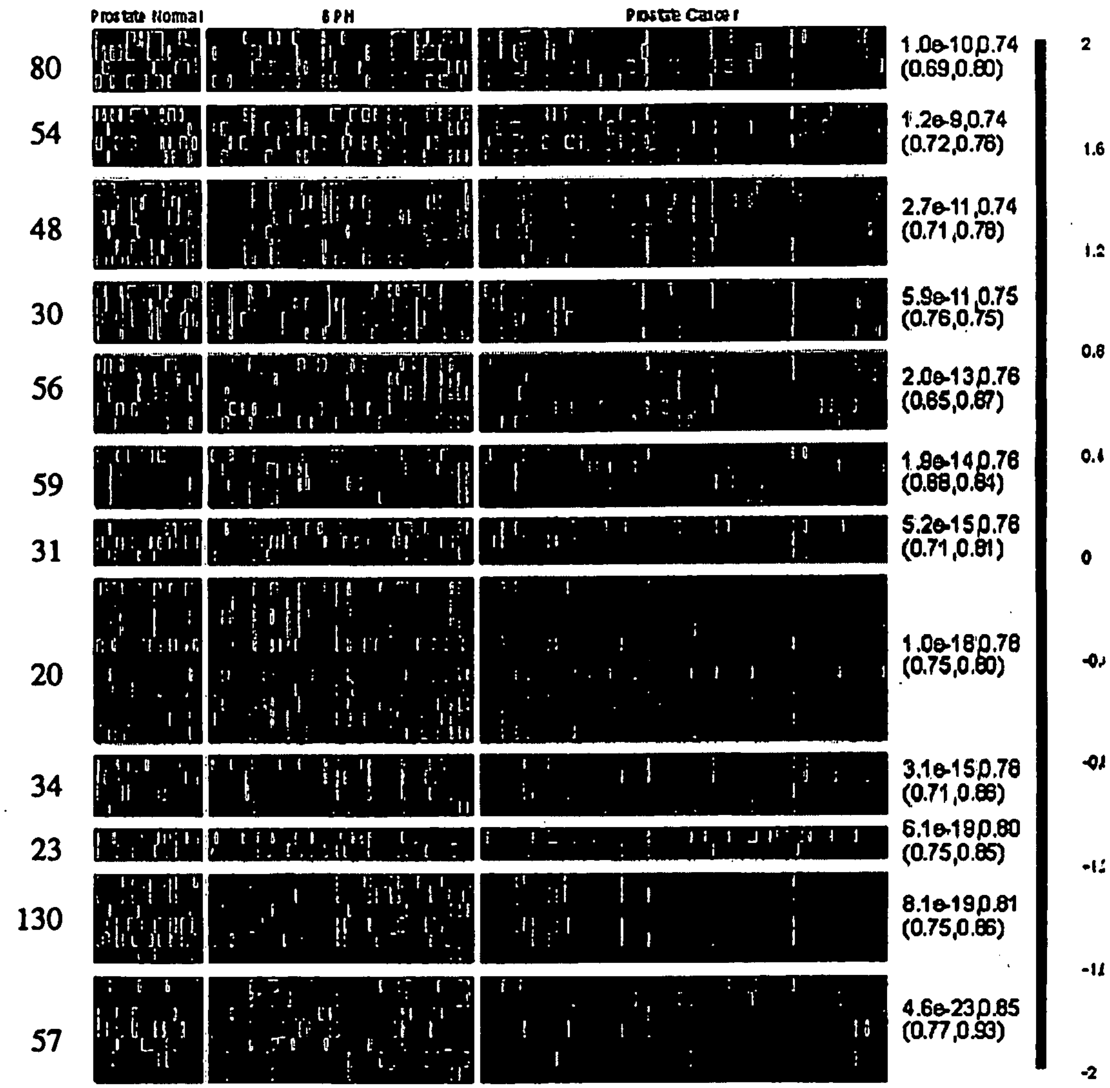
0.4
0.3

Figure 5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BPH
Prostate Cancer
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48
2.7e-11,0.74 (0.71,0.78)
30
5.9e-11,0.75 (0.76,0.75)
56
2.0e-13,0.76 (0.65,0.87)
59
1.9e-14,0.76 (0.68,0.84)
31
5.2e-15,0.76 (0.71,0.81)
20
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34
3.1e-15,0.78 (0.71,0.86)
23
6.1e-19,0.80 (0.75,0.85)
130
8.1e-19,0.81 (0.75,0.86)
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-2

Figure 6

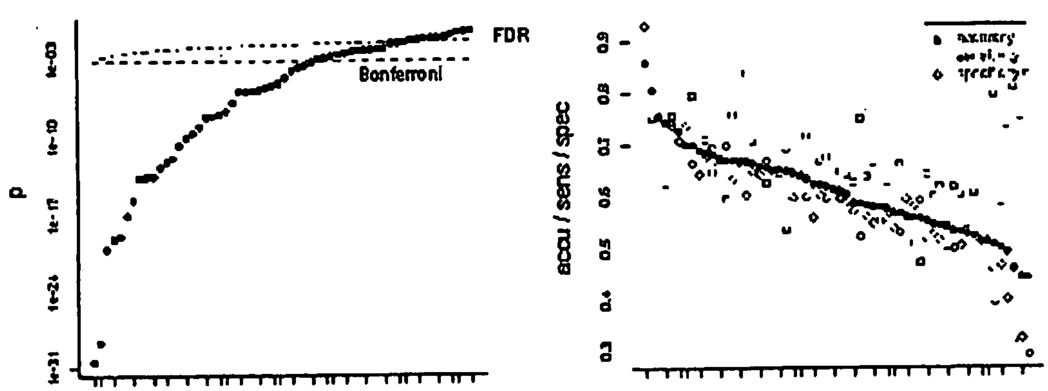
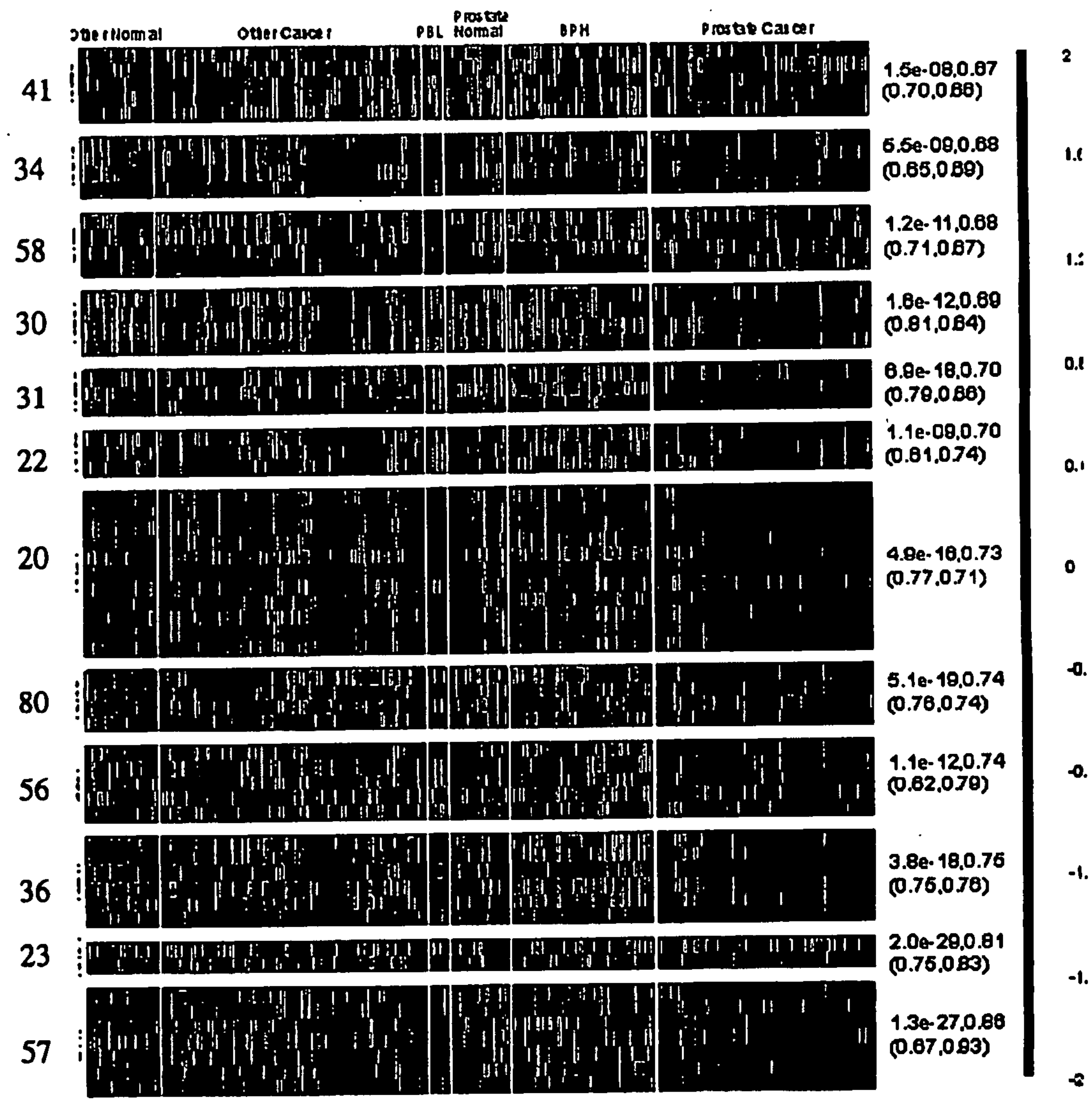


Figure 7



Other Normal
Other Cancer
PBL
Prostate Normal
BPH
Prostate Cancer
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34
58
30
31
22
20
80
56
36
23
57
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5.5e-09,0.68 (0.65,0.69)
1.2e-11,0.68 (0.71,0.67)
1.6e-12,0.69 (0.81,0.64)
6.9e-18,0.70 (0.79,0.66)
1.1e-09,0.70 (0.61,0.74)
4.9e-16,0.73 (0.77,0.71)
5.1e-19,0.74 (0.76,0.74)
1.1e-12,0.74 (0.62,0.79)
3.8e-18,0.75 (0.75,0.76)
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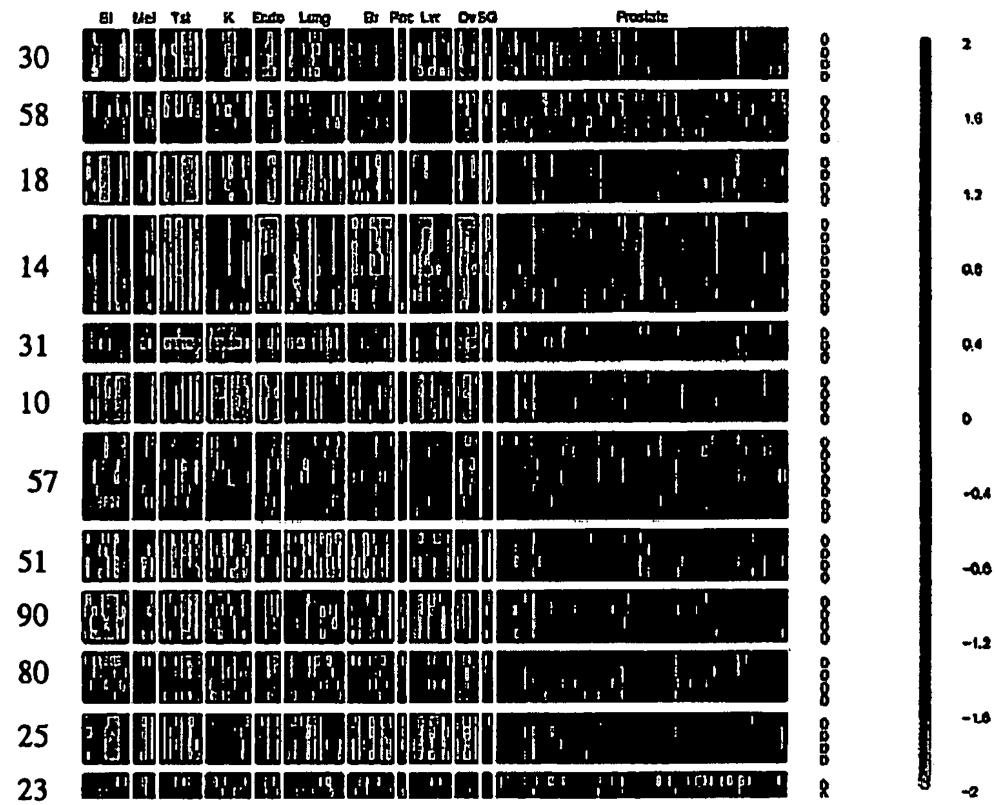
0
-2

Figure 8



Bl
Mel
Tst
K
Endo
Lung
Br
Pat
Lvr
OvSG
Prostate
30
58
18
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31
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57
51
90
80
25
23
2
1.6
1.2
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-2

EPO-BERLIN

21-07-2004

Sequence listing

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<400> 38

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<212> DNA
<213> Homo Sapiens

<400> 39

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<212> DNA
<213> Homo Sapiens

<400> 40

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gttggggttc gtggggtag 2299

<210> 61
<211> 2299
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 61

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tcgaggtttt atggttaat 2299

<210> 62
<211> 2428
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 62

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tgttattatt tttatttaat taattatttt gtatttttt ttgattaatt tttgaaaaat 300
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ttatgatagt tttagggtgg ttttttt 2428

<210> 63
<211> 2428
<212> DNA

<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 63

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tattgttcgt gtgaattggt tttttgagt ttttaaaaa ggattttaga ttttatttt 180
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tcgaatttgg tttttttta cgggcgagaa aggtatcggg tagggaaagg atttattagg 780
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tttaaggata gtttttaa atcgttgt 2428

<210> 64
<211> 2485
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 64

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taatattttt aagttagagt atatatgaaa tttttttt ttgttatta ttaagttttt 180

ttggttaggt gtagttgttt attttgtaa tttagtatt ttgggaggtt gagataggaa 240
gattgtttga gtttaggagt ttaagattag tttggataat atagtgagat tttatttta 300
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gtattattgt atttagttt ggatgataat agagtgagat tttgtaggta attaagtaag 480
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<210> 65
<211> 2485
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 65

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tgttttttag gtgattggtt tggggtaggt agtatatttg gttgttttta gtgggttttg 2460
agttgaagaa aggaggcggt aaaaa 2485

<210> 66
<211> 2528
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 66

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ttttgatgtt ttttgttttt tgggttagtg cgtatattat gtgagtgtgt gtgcgtgtgt 180
gtgcgtttc gttgggtgga acgaagagga gtgtgtgttt gttttaaaaa ttaaatcgcg 240
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tgatttttcg gggagttgtt gggggtgttt ttttttgga agggatggaa ggggggtcga 480
gaagatattg tttttatac gtgtaggggt taattggaaa ttggtttat ttatattttt 540
ttgttgttgt ttagttttaa tttagcgtag tcgtttttgc gtttgatttt agcggacgta 600
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tagttaggat ttaatttgga aattgattgt agaaggtgtt ttgttttgtt tgtatttaga 2460
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tttgtgtt 2528

<210> 67
<211> 2528
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 67

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tttagttatt tttgttttta taaaatttag gttataagtt tttgtattta gtggtatttg 180
ttattttg taaagaagta aattgttagg atttttttt tttagtgaac gtaggaagtt 240
tggagaaagt tgggggtggg gtgggggtta gttggagttt gggaggtttt tgttagtttt 300
gcggaaatac gttttatgg gtttagtttt gttttttt atagttttta aggaggaagt 360
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agtttttgag ttgagggata gggtatgtg gtttttta gtttgcgtcg gggataagat 720
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gttagatt 2528

<210> 68
<211> 2321
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 68

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ttaattgttt cggtggtgag gagttatggg gagtttttcg aagggttttt taggtagtgg 180
gttaatgggt aaaatgatta tttagtggtt ttgttgatcg atggtacgga tgtgttaagg 240
atatttatta gtttatttga gaatatgaaa taaagtgttg agattttatt atttaaagta 300
ataaagaaat cgtaagtaat acgattgata gttagaaggg aatattggag ttgtggcgtg 360
taatgttgtt ttggattagt attttaaat ttcgttaagt taaaggtttt gtttatttgt 420
gagtttttta tatgtataga attaggcgtg gttacgtaaa gtttttggat acggtttta 480
cgaagttggg agtcgatatt aggatgtcga tggtgtagat gatggtgaag atcgagaagg 540
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ttaagttcgg gtttttttcg gggggttgtt cgtcgtgtag gaggtgttta tcgtgcgtgg 720
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agtatttttg taagtttatt tatgtaaagt gtatgaaaag tgggtttttt ttttgaaatt 2220

atttagattt tgattttatt tatattttgt tttatgattt tggggaaatt ttattagtaa 2280
tttaataggt ttatttttta ttttaggaa ataaatatat a 2321

<210> 69
<211> 2321
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 69

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atttttata tattttatat ggatgggttt gtaagaatgt ttttttattt ggattgaggt 180
tttagttgtt tttttttt ttatgagagg taaaattagg ataaatttta tggtgatttt 240
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tttaggtggt taaatttagt ttattaagtg ttttgtaaa taagttattt tagaaaatat 360
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gtttatagta cgttagtatt ttaggaaatt ttttatagag ttttggtta aaagaaataa 600
tatttaaggt ttttttta aatagattaa aatattttaa taagtatttg tgttttaata 660
atgtagtatt tatggggtac ggtatcgttt tttaaatttt gggattagat tggagattat 720
taatttagtt tttgttttat atgaagtttt ttggtgtttg tttttatta gggtattttg 780
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aataaattag atttattaaa tttttttaa taattgattg g 2321

<210> 70
<211> 2412
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 70

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ttttcggtag ggagagacgg tcgtttagag tagcgagtgg ttaggaagtg tattttagtt 180
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gtttgtttt ttttagaac ggttttttga ttttagagat gtgaggatag gttgcgtggg 360
cggcgggttt tttatgggag tttgggttgg agagagtgtt gttttttttt tttttttta 420
tttaaggttg ttttattaa aattaaattt agtttttgt attattgtgt ttttggttgt 480
tggaataaaa gtagagagtt ggggaaggtt tttgatagat tgggcgtgtt tgtgagtttt 540
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ggtttgaggg tt 2412

<210> 71
<211> 2412
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 71

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gtttttttat gattaggtga gtgtttagta aataatttag tattcggtag agagagttag 240
aaatagtttc gaagagttta ggagaattta tttgttggtt tgaaagggga tatttaagtt 300
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gatattgggt tt 2412

<210> 72
<211> 2225
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 72

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tagtagttgt tatttatagt agtggtaatt tttcgtattt tttttcga aattaggata 180
tgtttggcga tgtttggaga tattttgggt tgttataatt aaggacggtg tttttaattt 240
tagtgggtag tagttaggga tgttggtaaa tattttagta tgtataggag ggttttataa 300
taaagaatga tttagttcgt aatattagga atgtcgaggt tgaggagttt tgtttcggag 360
tattgattta tgttatatgt tgggttttaa gagtttgttt aatttatata attttgtatg 420
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gataagaata aaaatttgtt ttaaaaaaaa aaaggaaatt tttttaaat tgaaaaaatt 1920
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cgcggtggtt tatatttgta atttagtat tttgggaggt cgaggagggt aaattatgag 2040
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gggcgtggtg gcgggcgttt gtagtttag ttatttagga ggttgaggta ggagaatggt 2160
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gcgat 2225

<210> 73
<211> 2225
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 73

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cgtttagtta atttttgt atttttagtg gaggcggagt tttatcgtgg ttttaatttt 180
ttgattttat gatttgtttt tttcggtttt ttaaagtatt gggattatag gtgtgagtta 240
tcgcgtttgg tttgttttg ggtttttttt tgattatggt taattgatta gaaggtttag 300
gataaagttt ttttagtttg aaaaaaaattt tttttttt tttgagatag atttttgtt 360
ttgtcgttta ggttggagtg taatggcgtg ttttcggttt attgtaattt ttgtttttt 420
gtttgaagcg atttttgt tttagtttt tgagtggttg ggattatagg tttattttg 480
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taggtgattc gttcgtttcg gtttttaaa gtgttgggat tataggcgtg agttatcgcg 600
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tgttgttgtt aagtttgtta tagttagtta gtggtggatt tgtttttaat atttatttag 2160
tagatatttt tttagtttgt atgtgattgg ggtttagatt taatttagtt tatagaggtg 2220
tatgt 2225

<210> 74
<211> 2205
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 74

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tttaaaagtt taagtatatc gtggagttga atgaaaaata gtttttgaa taattattat 120
taaatgagta aaagtttaaa aataatgtaa aaagttaaag tcggttgggc gcggtggttt 180
acgttcgtaa ttttagtatt ttgggaggtc gaggtgggcg gattacgagg taaggagatc 240
gagattagtt tggttaatat ggtgaaattt cgtttttatt aaaaatataa aaattagtta 300
ggtgtggtgg tgagtgtttg gtggtgagtg tttgtaattt tagttattcg ggaggttgag 360
gttcgaaaat tgtttgaatt taggaggcgg gaggtgtag tgagtggaga tcgtattatt 420
gtattttagt ttggcgatat agcgagattt cgttttaaaa aaaaaaaaaa gttaaagtcg 480
tttgagtaaa taaaagatta gataaaaatt ttatgaatta aaaattagtt ataaagttgt 540
ttaattagaa taggatgagg aagaaaaggg gaaatcgatt atttttgatt aagtgtaaat 600
tttaagtaaa ttattgatat taatagtgag ttggagtatt ttgttttatt aggtaatttt 660
ttgtaaatat tttgtaacga ttttatatat ataaagtttt tttatgtttt tttttaaaaa 720
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ttttattttt tttttggtt attatgaatg ttttttata attggagagt taggatgaat 840
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ggaaaaagat ttagaggaga gtagcggtat ttttgtttta gttttaattc gaacggaggt 960
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ttaatataat tttgacggtt attgatgtta aagatcgttg ttgaaagttt taaatgggga 2160
gtgagtaatt ttaattttg aattggttgt tttgagttaa ggtta 2205

<210> 75
<211> 2205
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 75

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ttgttttaaa ttacggttat gtgtttggta agggtgttgg ttaatcgaaa atgttggttt 180
tagagttaga agtattggta tttaaataaa tatatttggg ggttgggggt tgatgagtaa 240
ggttgggagg agataaaaga agtatttcgg tttagtcgtt agagacgcgt aaggtgtaac 300
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aaaattgtcg tttattcgcg cgattatcgg taaagtagtt ttatagtttg ttttttttt 480
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tgtggggaag ggagaaggat ttgtaaattt cggagcgagg ttttgtttat tcgaggtcgt 660
tgttgtgcgg agatttcgg gtgaagttat cgttattatg tttgattagg tatcgggttg 720
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<210> 76
<211> 2355
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 76

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cgagttttat cgggttattt ttgtagagtt gcggttatat gttttgttag gtgttaggaa 180
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gaggatcggg tagttttttt agggtttgg acgagattcg gttatggatt ttagtttatt 660

gaagtatttt tatagtttgg gtttgcgga tggacgttat ttagggtagg gtttgtagta 720
tggtttagtt acggatttgc gttattttat agatttttg gtttattcgt tttttatgcg 780
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gattgtcgat agtag 2355

<210> 77
<211> 2355
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 77

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ggtgttttat aggttgtagg aaagggagtt ttttgtcgtt gtttttgttt ttttagttgt 360
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<210> 78
<211> 2380
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 78

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<210> 79
<211> 2380
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 79

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<210> 80
<211> 2308
<212> DNA

<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 80

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<210> 81
<211> 2308
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 81

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<210> 82
<211> 2352
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 82

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tttagttagg ga 2352

<210> 83
<211> 2352
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 83

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aggtttttt ttttaagggg attttgattg gatgggtagt atgagtgttt attttaatat 240
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taggagtcgt tt 2352

<210> 84
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 84

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ttttatagt 2229

<210> 85
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 85

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gtttgtggtt attattggga taaaagagaa gttagttcgg aggttagttt attgttgttt 240
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<210> 86
<211> 2280
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 86

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aaaagtagga tattaaattt gttattttta gagggttttt tagtttttt ttttattttt 180

gaattgagcg aagcggtgtc gattttatt tttgggtac gagttttgc gtatttggga 240
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<210> 87
<211> 2280
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 87

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<210> 88
<211> 2438
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 88

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<210> 89
<211> 2438
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 89

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<210> 90
<211> 2403
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 90

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ttg 2403

<210> 91
<211> 2403
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 91

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ttaatatttt ggaatgggga tgagggggta gttagttttt gtttttagta agagagatgt 180
aatagggttt tgtggttgag ttgggtgttt tgttttatat ttgtaatttt aatttttgag 240
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ttt 2403

<210> 92
<211> 2311
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 92

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ttggttatta gagattttcg ggagttagtt tgtagggtag gagtataatg acgtggttag 180
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<210> 93
<211> 2311
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 93

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gaaaatttgg tgtgtttttt ggtgttatag a 2311

<210> 94
<211> 2271
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 94

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tattgttttt ttaagaatgt gtatagtttt agagtttgaa ggtttaaaat atagggtata 240
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<211> 2271
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 95

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<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

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<211> 2546
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 97

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<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 98

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<210> 100
<211> 2413
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 100

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<210> 101
<211> 2413
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 101

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gtaggtagag gttattttg ttaggttggg gttgtatggg ttggagattg ttttttata 180
tttgagatat gatttttaag gatttgttgt tagttatggt gataggttgg ttggggttgg 240
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<210> 102
<211> 2222
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 102

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gttaaaatat tatattgtgg gtgggaggtg ggggttggtt tgaaggagga tggatagtga 240
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aaagtagttt gataaaaggt tttatatatt taatattaga gattagaaat agattaaaaa 540
aaaaaaaaaa aaaaaatata tattatataa ttggtaaatt tattaattta ggtttattta 600
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tt 2222

<210> 103
<211> 2222
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 103

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gtggcgagtg gttggtgggt aggtttattt gttgacgagg tttttttcgg gttttaggaa 420
aaggggggaa tttggagtag gtcgtttagt ttggtttggt ttttacgtcg tggtgtatat 480

tttcggggtt tggtttgttt tggtttgttc ggagggttag tttttttaga attggttgcg 540
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ag 2222

<210> 104
<211> 2162
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 104

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ggtgtttgcg cgtttgtggt tggattggа tgtgttaggg atgggaaaat ttattatgtt 180
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<210> 105
<211> 2162
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 105

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gttggttagt tttcgtgttt tgtttttgtt tgtttttgtt tagcggtaaa tagggatttg 180
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ttgaaagtag ttattaaatt gagtattttt ttgttttag attttaata ttttttgt 300
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<211> 2586
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<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 106

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tggggt 2586

<210> 107
<211> 2586
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 107

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<211> 2257
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 108

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<210> 109
<211> 2257
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 109

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<210> 110
<211> 2352
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 110

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<210> 111
<211> 2352
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 111

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<210> 112
<211> 2470
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 112

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tataaagtat taaaaatatt ttttagtagt tttgtttaag tattttaggt tagtggtagt 240
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<210> 113
<211> 2470
<212> DNA
<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 113

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<210> 114
<211> 2305
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 114

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<210> 115
<211> 2305
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 115

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<210> 116
<211> 2234
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 116

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gagatggtac gtgtgtacgt tgttgatggt agcgtggtgt gtagtagtag aaagttggaa 1920
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tttttttat agattgtttt gtgttattcg atgagtaaat tgtatgcgtg ttatttgttt 2160
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gttttgggat cgag 2234

<210> 117
<211> 2234
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 117

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tagtgagttt gtgtgtatat ttaaggtggt ataggatgtt ttttttttt ttacgtttt 240
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aaggtagtaa gtgg 2234

<210> 118
<211> 2317
<212> DNA

<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 118

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gtggttttat ttttagttt ttagagttat aggttaggag cggagggtta aggttggcga 240
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aatggagtcg ttttggttg gggaatttta ttagggt 2317

<210> 119
<211> 2317
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 119

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aggaataagg ggaaggaaga gagagggagt aggcggagcg agagagggag aaataggcgc 240
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<210> 120
<211> 2553
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 120

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<210> 121
<211> 2553
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 121

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<210> 122
<211> 2381
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 122

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<210> 123
<211> 2381
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 123

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<210> 124
<211> 2514
<212> DNA

<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 124

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aaggaacgta ttgaggaacg tattgaggat tagaagttag aatttttgaa tttgtaaatt 240
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<210> 125
<211> 2514
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 125

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tatttttag gagttttttt gtaaagggtt aggtagggtt tgttgatatg tagagaacgg 180
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<210> 126
<211> 2325
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 126

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tggcggattc gcggagattt tattgtttta ttatgggtag ggcgggggttt tggggtattt 180
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cgtttttcg tttggtttaa agggaggcga ttagatagtg taagttttta ttttttttta 600
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aaaataaaaa gttagggata ggaagtattt tgtttaaaga tttat 2325

<210> 127
<211> 2325
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 127

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<210> 128
<211> 2541
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 128

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ttttgttcg tttagtgttt a 2541

<210> 129
<211> 2541
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 129

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<210> 130
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 130

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<210> 131
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 131

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<210> 132
<211> 2257
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 132

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<210> 133
<211> 2257
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 133

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<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<220>
<221> unsure
<222> (1598, 1841, 1846, 1848, 1869, 1871, 1873, 1874, 1878, 1880)
<223> unknown base

<400> 134

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<211> 2434
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<220>
<221> unsure
<222> (555, 557, 561, 562, 564, 566, 587, 589, 594, 837)
<223> unknown base

<400> 135

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<210> 136
<211> 2476
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

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<210> 137
<211> 2476
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 137

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<210> 138
<211> 2520
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 138

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<211> 2520
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 139

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<211> 2555
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 140

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<211> 2555
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 141

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<211> 2516
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 142

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<210> 143
<211> 2516
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 143

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<210> 144
<211> 2364
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 144

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taagagttaa gtttaggtgc gttataggtt gaaatataaa cgttaaaggt ttataaggta 180
gtttttatgg tagggtaaga gtttttatt ttttgttgg tttttgttt tgttttgaga 240
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aagtgttggg attataggcg tgagttatta cgttcggttt agattttga aacgttaata 540
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tgaaaagtta tagaatggaa gatatttata tttttgtat attgtttttt aaaaatgtat 660
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tttgtgggaa atttttttta tttt 2364

<210> 145
<211> 2364
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 145

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gagttaatt tttgtttg tattggaagt gaattgattg tatatatagt tttgttata 180
tatatatgtt tttttgaaa gtattagttg tgtaaagagt ttagaaatgt ataggagaga 240
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aggtgtattt tgcgttagtg tttattagtt ttgttcgttt ggagtttata ggtcggttag 420
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gttgtttggt agtgttagtt ttgt 2364

<210> 146
<211> 2408
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 146

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agaggtcgat atagtttagt tttggggttt ggttttattt ataagaggtt atattttgtt 180
atagtattgt ttatttggtt tgttttagaa gtatcgttag agtggcgaag gtaggaggtg 240
gtgtacgaga gtttacgttt tagtatttat ttaagtgagg gaaaggcgtt tcgtatttag 300
aaaaatgtaa aattaatgat ttttatttat atatgagatt gtggatttat ttatgtatga 360
gatagtggat ttagagttat gttgtggttt ttatttgttg ggagttagta gtgtttgtgt 420
tttggtttg ttttttagt tatatggttt atgtgaggtg cggattattt tgagttgttt 480
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ttagaagaaa atattagaat tggggtgtgg tggaaggatg ggagtataat ttgggagggg 600
aagatttgtt tttttttat atattaggag ggagtggtag gaaggggaga tattgtgtcg 660

gatttaggga gttaagagcg tgagtatttt taggttttaa ttgttgaac gttgtgtatt 720
tgggggcgtt cgtgtagtag gaatatttt ttattataa ttttttggg tatagtggag 780
agttatgagt gggggttgtt ttggggggttg cgttatggtg agtgagttta cgttaggagt 840
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ggggagtg 2408

<210> 147
<211> 2408
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 147

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agggagagtg tttatcgttt ttagtagttg ttatttttt tatgattaaa gcgggaggag 180
agcggtattt tcgtatagat tattttgaa gcgaggggta gattttaaga gttttttaga 240
gtttgagttt tgggtttgtt atcgcggggt ttaatgtata attagggttt tttgaaaatt 300
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ttatgtgt 2408

<210> 148
<211> 2523
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 148

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ttttttttt tttgatagat ttttatttg tggtttaggt tggagtgtag tggcgtgatt 180
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tta 2523

<210> 149
<211> 2523
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 149

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gag 2523

<210> 150
<211> 2280
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 150

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<210> 151
<211> 2280
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 151

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aagcggtgtc gatttttatt ttttgggtac gagtttttgc gtatttggga gatttttgaa 240
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<210> 152
<211> 2413
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 152

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<210> 153
<211> 2413
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 153

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<210> 154
<211> 2171
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 154

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ttacggagga g 2171

<210> 155
<211> 2171
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 155

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cggaggaaat cgtttatttt ttgggtttcg gaatcggggc gaatgggtgg tgtttcgtcg 180
gtcggcgcgg cggttgtggg tttagtttt agttcgcgtc ggacgttgat cgtttttcg 240
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ttttttttt g 2171

<210> 156
<211> 2490
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 156

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cgttatagtt atttttttt tttttggg tatcgtttgg attcgtttat tatagattat 180
tatatttacg gttattatgt ttatagttat atttttttt attttagaga ttgtttatat 240
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aattattata tttataatta gaggttttac ggtgattttt tttttatttt cggggattat 480
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gattatagtt atcggtttta ttattaattt ttttaatt ttagggataa tttttatttt 660
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gtttttagt agttttata cggtgcgtat 2490

<210> 157
<211> 2490
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 157

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gatgggggag tattattggt ttgtgtgtta gaggagggtg ttgttataga attagtggtt 300
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ggggttatcg tggagttatt ggttgtgggt gtggtggttg tgttgattta tattggaggc 420
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atgattgtgg gtgtggtggt cgtgttggtt 2490

<210> 158
<211> 2418
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 158

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gagggttttt ttggtcgagg ggtttgttgt ggcgttggag gggtaggggt ttattgtttt 180
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cgttttgttt ttttgga 2418

<210> 159
<211> 2418
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 159

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<210> 160
<211> 2351
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 160

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<210> 161
<211> 2351
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 161

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gaggtcggtt t 2351

<210> 162
<211> 2427
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 162

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<210> 163
<211> 2427
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 163

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<210> 164
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 164

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<210> 165
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 165

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<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

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Figure 1

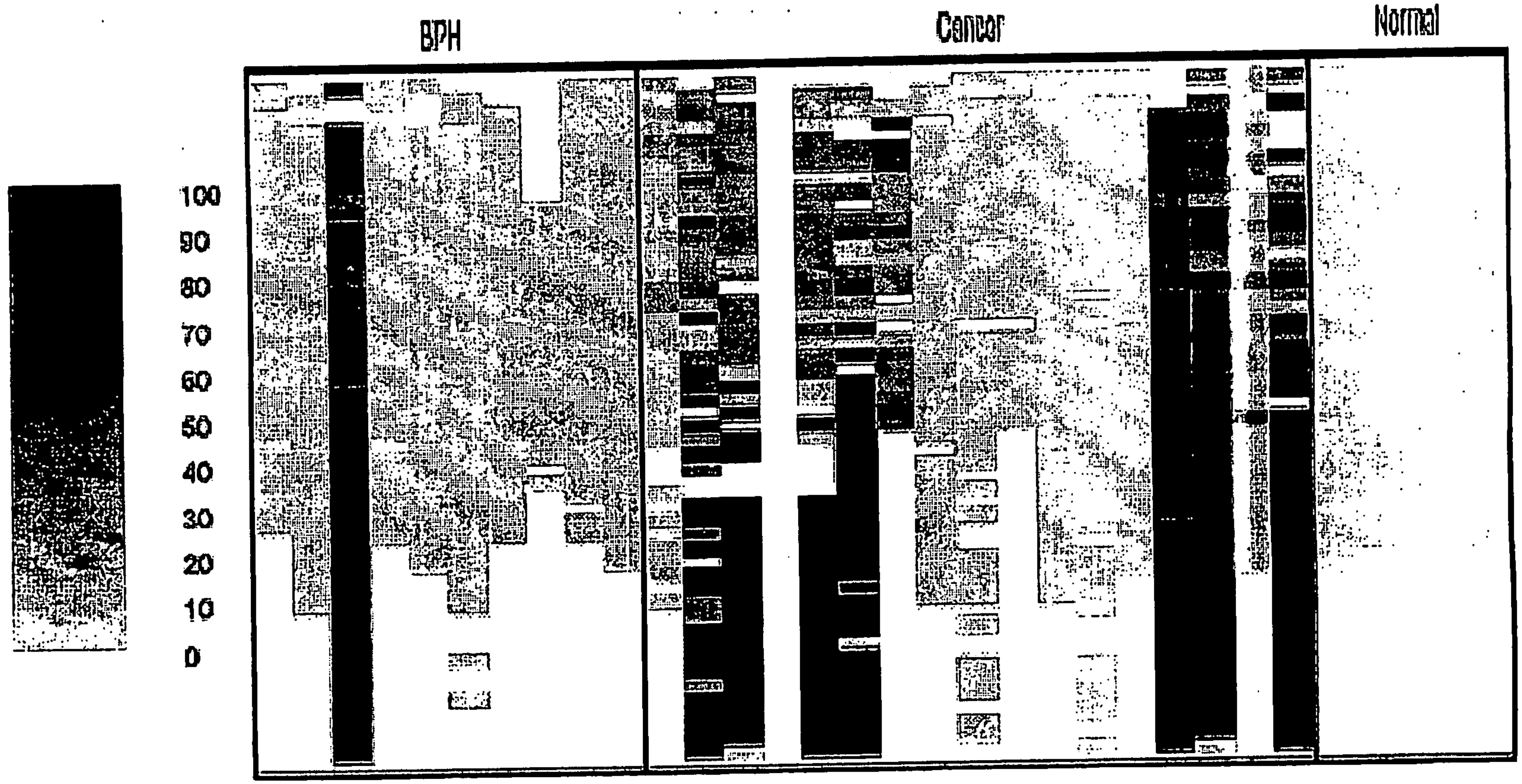
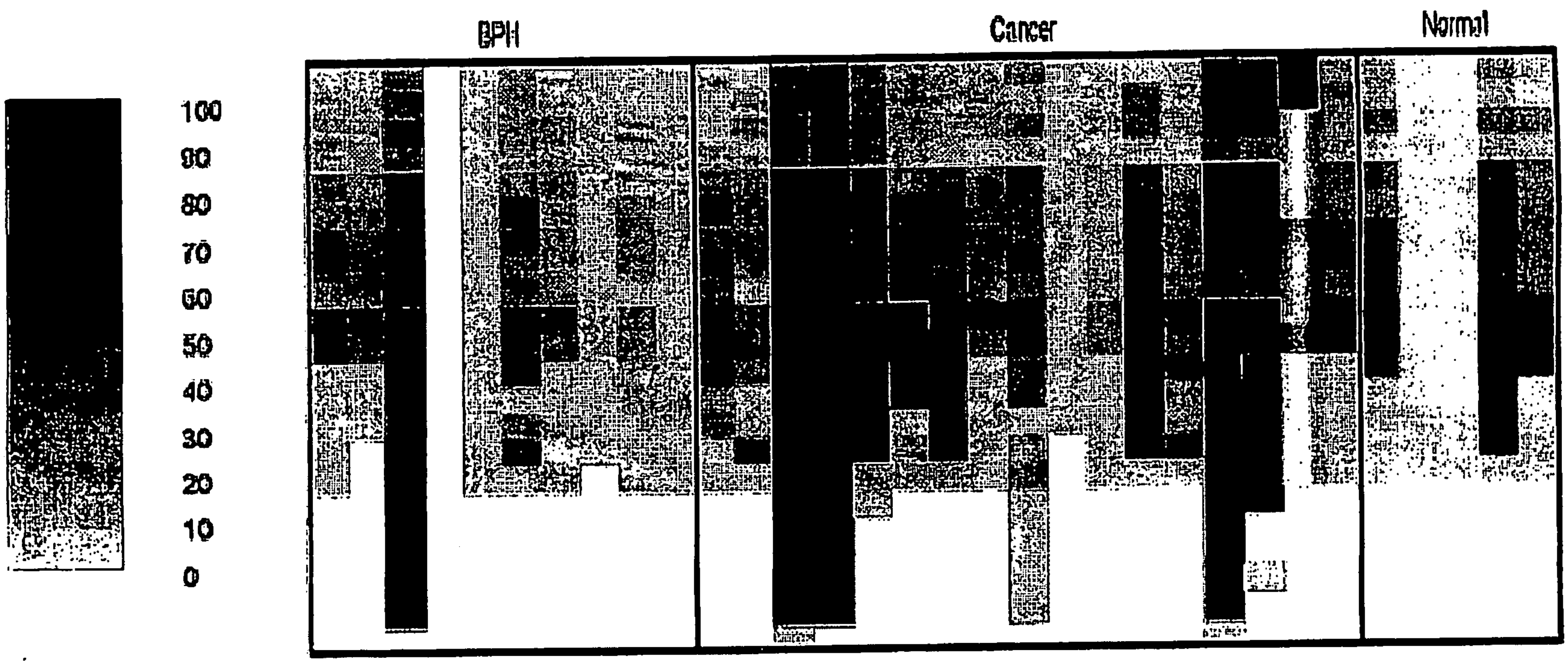


Figure 2



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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

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<213> Artificial Sequence

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<223> chemically treated genomic DNA (Homo sapiens)

<400> 170

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<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

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<210> 172
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 172

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<210> 173
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 173

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<210> 174
<211> 2501
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<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

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<210> 175
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

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<400> 176

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cgattgtgcg gatcgttcgt tattagtcgt tttttaaatg cgtgtagaat ggaggcgaaa 5700
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ggttaggcgc ggaggaaaga agggttcgcg gcgttgtaag gcggaggaag tagaggttcg 5880
cggtgcgttg gggttttgtt tcgacggtcg ttttaggtt gtgaaagttt gggttgtttg 5940
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atgttgtat 6009

<210> 178
<211> 2299
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 178

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tttttttttt gtggtttttt tgttttatt aagatagttt ttaggatttg ggggatagtt 180
agtttgaggt tttttttaa atgaaagaag tttagtttgg ttttaggaa gtgtgtggat 240
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ggtatttttt tagatgtttt gagttagggg gttttgaggg aaaattatta tgtttatttt 480
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gttggggttt gtggggtag 2299

<210> 179
<211> 2299
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 179

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taggttgtat ttttggtagt tttttgtggg tgggtaggta ggtaggtagt ggatgtagag 180
gttattgggg tgagagttgg ggttgttttg gttttttgt ttttggttgg aatgtgagtt 240
gtaggggtta tttttaggt tttgtttttt ttttatagtt atttattagt tttaggttta 300
gttaatttgt gatttttagt tttgttaggt ttttgtagtt tgggagttgg atatagaagg 360
tagtgagagg agtggtggta aagaaagatt tagaattaag ggagggtata tataaatgta 420

gagagagagg tatagttttt atttatagag atagatatat atatgtagag ataggtaggt 480
gtgtagattt atagttttat tgaaagatat atatttagat atttttaaat atatttagat 540
atatagtgga tatgaataga ttatataagt atatagagat atagagagat ttgattttta 600
tatagaggtg tatttggagg tatagtagtt atatgtattt agattatata gaggtttaga 660
tgtattgttt atggatattt atagatttgt aaatgtttat gtatatgtgt agatgtatat 720
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ggttttgtta aaagtatttg tttattaatt ttaggtgggt ttttggtttt gtggttaggg 2280
ttgaggtttt atggttaat 2299

<210> 180
<211> 2428
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 180

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gtagtgattt taggggtttt tgtatatttt atattaattt tagaaatatg tttatgatta 180
ttttattaaa attattaatt gttatataaa tatttgtttt tttatgagtt gtaaaataat 240
tgttattatt tttatttaat taattatttt gtattttttt ttgattaatt tttgaaaaat 300
aatatttaat attaaaggta ttttttttta tttagggttt tagatagtaa gatgtttttt 360
ttttaaatag taagatgttt ttttaagttt tatggaaagt atttttttga tattagtttg 420
gggaggttga attttggagt ttttatttga agagtaaagt attgtattta gtaatgtgtg 480
ttttgggaat taagtttaag tagttttggt tgtttttttg tttaggttgg tattgtttgt 540
gtttgttagt tttttgtga agttagttta tttgtggatt aggttaaatt tttggagatt 600
ttatgtagat gtgggtgtag tttgttttgg gatttgaagt ttgttggagt ttgagttttt 660
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ttttgggaaag tgtgaaagtg ttatgtgttt tgtattttgt ttagttgttg tgtagttttt 900
ttttggtttt tattgggaga taggggattt ttatgagaag gaaggagtag ggtagtgatt 960
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gaattagttg agtgtggtag tttttattt gttgttgttg tttaatatta tatgtgttta 1920
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ttagaggaat taatttatat gaataataaa agtttattt gagttaaaga ttttaattta 2340
gaaatgagaa aatggggatt tttaaaaggg ttatagggag agggttggag gaaagttaga 2400
ttatgatagt tttagggtgg ttttttt 2428

<210> 181
<211> 2428
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 181

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tattgtttgt gtgaattggt tttttgagt tttttaaaaa ggattttaga ttttattttt 180
atagattttg atttagtatg ttggggtgtg gttatggaat ttgtattttt atttgtttta 240
ttttataatt tttgttttaa atttgtatta agtttttga atagttgttt ttgttattgt 300
aggatgattt taatgttttt ttaaagtttt agaattaatt aaggtaattt gtgtttgaag 360
ttgtgtttgt ttatagaaat agagattgga tgttagtaat tattgtgtta taagatggga 420
aatgaattta gaagtgttat tttaatttga atttttaatt gttaattatt atattttaat 480
ttgtgtttat gggagaaatg tagtttgtta ggtatatgta gtgttgggtg gtaatagtaa 540
ataggagatt gttatattta gttggttttg gaaagtttta tttttttta ggaattttg 600
tttttttaatt atgtgtttta aaagatttta aggagtattt ttatattata ttttaggtat 660
tttgagtagg agtttttta ttttattttt tgattagtga atagtttttg ttttgtttaa 720
ttgaatttgg tttttttta tgggtgagaa aggtattggg tagggaaagg atttattagg 780
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gtataatttt tggtttttga agttgagatg ggaagggaat tataatgggt ggttgtttag 900
tttttttattt aaaatttttt tgattttggg ttgaggtttt tttgtttatt gtttttgtta 960
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ggatgaagat tttagagttt ggttttttta aattgatatt aaagaagtgt ttttatggg 2040
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gaaggagatg ttttttagtat tgggtgttat ttttagaag ttggttaaag aaggatataa 2160
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gagtaaattt tggaagtata attgtaaaaa taatgttata tagttaagga gaagagaaaa 2400
tttaaggata gtttttttaa attgttgt 2428

<210> 182
<211> 2485
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 182

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ttttaaatta attatttaag agatattatt tttgttagtt tattttagt tttttatgt 120
taatatttt aagttagagt atatatgaaa ttttttttt ttgtttatta ttaagttttt 180
ttggttaggt gtagttgttt attttgtaa ttttagtatt ttgggaggtt gagataggaa 240
gattgtttga gtttaggagt ttaagattag tttggataat atagtgagat tttattttta 300
taaagaatta aaaaaaaata agttgggtat ggtggtatgt gtttgtagag ttagttattt 360
aggaggttga ggtgggagga ttgtttgttt aggaggttga ggttgtagtg aattatgatt 420
gtattattgt attttagttt ggatgataat agagtgagat tttgtaggta attaagtaag 480
taagtagttt ttttaatgtt ttgataggtt ttgagttggt taaatgtaag tgatggtgat 540
tgattttttt gttatagtaa gttttgaata aataaagtat ttgggtggtt tttttttg 600
atttttttta tttatttatt tgtttattaa ttatatatta gttgtgtttt atttgttagg 660
tagtggttag tattgggaat atgtggaagt aaatagtttt tgtttttaag gatattttgt 720
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tattgaaggg aatttatggt taggtaaggt tgtatatttt tttttggtt gggagtatgg 2280
tagaggatgg taggtaggtt ggggggtttt gggaggttgt tttaagtgag gtttgttttg 2340

gagttgtatt tggatttgt attttggtta gttggatgta gagatgatta aagttgtatt 2400
attttgaggg ttgataaata atagttttta gtttatagat taggagtggt agagtgagtt 2460
ggtttgttta gttttgtaaa gtgta 2485

<210> 183
<211> 2485
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 183

tgtattttat agagttgagt aagttgattt attttattat ttttggttta tgggttagaa 60
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agaatataaa gtttaagtgt agttttaggg taaattttat ttgggatagt tttttagggt 180
tttttaattt gtttgttatt ttttgttgtg ttttttagttg gagggaaagt gtgtagtttt 240
atttagttat gggtttttttt tggtggtttt aatgtttgtt atttttttt ttttttgttt 300
tgagaaggtg gtttttttgt tttaggtatt ttttatgttt gtagtttaga aagatttgat 360
tttaggtttt tgtttgattg agtttatgag ataaatttgt atgggaattt tatggttttt 420
attttttttt taggttttg ttttgtttgt tttggtttt taggtttagg ggattttatt 480
tgggtatttt gggagtgggg tgttttgtg ggttagtttt gttttttagg aattggttgt 540
ttttaggtgg tggggtgtgg gttttgtttt tttttttgt ttttttgggt tttatagttt 600
ttttgtgttt atatttatgg gattaagtgg tttgttggtt tttttggtat ttttggttt 660
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<210> 184
<211> 2528
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 184

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gtgtgttttt gttgggtgga atgaagagga gtgtgtgttt gttttaaaaa ttaaattgtg 240
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tttgtgtt 2528

<210> 185
<211> 2528
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 185

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tttagttatt tttgttttta taaaatttag gttataagtt tttgtattta gtggtatttg 180

ttatttttg taaagaagta aattgttagg attttttttt tttagtgaat gtaggaagtt 240
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gtggaaatat gttttatgg gtttagtttt gttttttttt atagttttta aggaggaagt 360
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tattagaagg aattttggtat ataatttatt tgtttttaga gtggtattgt ttagtatttt 2460
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gttagatt 2528

<210> 186
<211> 2321
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 186

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ttaattgttt tggtggtgag gagttatggg gagtttttg aagggttttt taggtagtgg 180
gttaatgggt aaaatgatta tttagtggtt ttgttgattg atggtatgga tgtgttaagg 240
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ataaagaaat tgtaagtaat atgattgata gttagaaggg aatattggag ttgtggtgtg 360
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gagtttttta tatgtataga attaggtgtg gttatgtaaa gtttttggat atggtttttta 480
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tgtttttgtt ttggtagtgg aagtggttgg taatgtagtg gatttttttt aggatttgg 660

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tttaataggt ttatttttta tttttaggaa ataaatatat a 2321

<210> 187
<211> 2321
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 187

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atttttata tattttatat ggatgggttt gtaagaatgt tttttattt ggattgaggt 180
tttagttgtt ttttttttt ttatgagagg taaaattagg ataaatttta tggtgatttt 240
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gtttatagta tgttagtatt ttaggaaatt ttttatagag ttttggtta aaagaaataa 600
tatttaaggt ttttttta aatagattaa aatattttaa taagtatttg tgttttaata 660
atgtagtatt tatggggtat ggtattgttt tttaaatttt gggattagat tggagattat 720
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aataaattag atttattaaa ttttttttaa taattgattg g 2321

<210> 188
<211> 2412
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 188

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ttgtagggag tgggtttggg tgtatatagt tgtgggtagg tgtagaggtt atgatagttt 1980
gaaggtaggg tttttttgt gttgtgtgat gaggttagta gttttaggta ttagttttat 2040
gtgtgtttta gaagtaattt tggtgttgaa agggttttag tagtttgggg ttttgtttag 2100

ttgttgatat aggatttagg tgttttttt taggttagta ggtaggtttt tttgagtttt 2160
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ttatggggag atagaatttg tagttttttt tttatttttt gattagttta ttttataata 2280
gagattagtt ggataagttg ggagtttttt ttttttatg ttgtttggga gtaatttgaa 2340
ttttgtttt ttttaggtt tttttgtg aaagtgttgt ttttttttg ttttgtagt 2400
ggtttgaggg tt 2412

<210> 189
<211> 2412
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 189

agtttttaga ttgttgtagg ggtaggagaa aggtagtgtt tttatggagg ggggtttgga 60
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ttagttgatt tttgttatga ggtgagttga ttaaggggtg gggagagagt tgtaagtttt 180
gttttttat gattaggtga gtgtttagta aataatttag tatttggtag agagagttag 240
aaatagtttt gaagagttta ggagaattta tttgttggtt tgaaagggga tatttaagtt 300
ttgtgttagt aattggatag aattttaggt tgttgggatt tttttagtat taaggttgtt 360
tttgagatat atatgaagtt aatgtttggg attgttggtt ttattatata gtgtaaagaa 420
agttttgttt ttaggttgtt atggttttg tatttgttta tagttgtgtg tatttaggtt 480
tatttttgt aattttggg gagtagttgt ttttattaaa gggttttagt tttgtttta 540
ttatttttt aagtattggt gataaatggg atttttataa ataattgttt ataagttgag 600
aataatggta ttaaattttt atgtttagaa gttgtagtgg tatattttt tgaaattagt 660
aattggatgt ttttttttgt ttaatttagt agattttaaa gtatttggag atgttgtttt 720
taaattttt tatttgggag gtttaggttt ttgttttgag ttttgtttat gtttttttag 780
tatgaaattg tatagtgttt tgttgaggtt tgatgaagga tggttttaaa attataagaa 840
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tatgtatatg tttttggtgg aggggttatt gttgttagag atattttttt atttttttat 960
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gtttttgttt taataattag gggtataatg atgtaagagg ttaaatttga ttttaatgag 1980
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gatattgggt tt 2412

<210> 190
<211> 2225
<212> DNA

<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 190

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gtttgttagg taagtgttga gggtaggttt attattgatt gattgtggta gatttggtaa 120
tagtagttgt tatttatagt agtggtaatt tttgtattt ttttttga aattaggata 180
tgtttggtga tgtttggaga tattttgggt tgttataatt aaggatggtg ttttaattt 240
tagtgggtag tagttaggga tgttggtaaa tattttagta tgtataggag ggttttataa 300
taaagaatga tttagtttgt aatattagga atgttgaggt tgaggagttt tgttttggag 360
tattgattta tgttatatgt tgggttttaa gagtttgttt aatttatata atttgtatg 420
gtgggtggtt atttttattt tttagatgag gaaattaagg attagagagg ttaagtaatt 480
gatttgaagt taaatagttt atgagtggta gagttttatt taaatttga gtatatgttt 540
ttagttaaag ttttgtattt ggtagatagg tttaatgata atgtatgatg ataattagtt 600
tgggtattgt ggtggagtgt tgtaggtttt taatagtatg gagtaggtga aggggttttg 660
taagttgtgt aaatgatgat gttgttattg gttatattat tgggtgagtt attgtgtaag 720
aattgtattt aggttatatt tttgtgtttt tagtagttgt ttggttttg gttttagaga 780
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tggttgatat ttttatttaa ggatttattg tggtggtttt ttagtattag tgaaattttt 1260
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taagaaagta ggtttggata ttgtagagag gttgataaaa tttgaagttt agtgggtttt 1560
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atttaaggtt aggagtttga gattagtttg gttaatgtgg tgaaatttg tttttattaa 1740
taatataaaa ataagtttgt aattttagtt atttaggagg ttgaggtagg agaattgttt 1800
taaataggga ggtaaaggtt gtagtgagtt gagagtatgt tattgtattt tagtttgggt 1860
gataagaata aaaatttgtt ttaaaaaaaa aaaggaaatt ttttttaaat tgaaaaaatt 1920
ttgttttagg tttttgatt aattaattat aattaaaaga aaatttagag ataggttagg 1980
tgtggtggtt tatatttgta attttagtat tttgggaggt tgaggagggt aaattatgag 2040
gttaggagat tgagattatg gtgaaatttt gtttttatta aaaatataaa aaaattagtt 2100
gggtgtggtg gtgggtgttt gtagttttag ttatttagga ggttgaggta ggagaatggt 2160
atgaatttgg aaggtggagt ttgtagtgag ttaagattag gttattgtat tttagtttgg 2220
gtgat 2225

<210> 191
<211> 2225
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 191

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tttatgttat tttttgttt tagtttttg agtagttggg attataggtg tttgttatta 120
tgtttagtta atttttgt attttagtg gaggtggagt tttattgtgg ttttaatttt 180
ttgattttat gatttgtttt ttttggttt ttaaagtatt gggattatag gtgtgagtta 240
ttgtgtttgg tttgttttg ggttttttt tgattatggt taattgatta gaaggtttag 300
gataaagttt ttttagtttg aaaaaaattt ttttttttt tttgagatag atttttgttt 360

ttgttgttta ggttggagtg taatggtgtg tttttggttt attgtaattt ttgttttttt 420
gtttgaagtg atttttttgt tttagttttt tgagtggttg ggattatagg tttattttg 480
tattattagt agagatggag ttttattatg ttggttaggt tggttttgag ttttgattt 540
taggtgattt gtttgtttg gtttttaaa gtgttgggat tataggtgtg agttattgtg 600
tttggttaaa aatttatttt tgtaatgagt ttttttttt aattagttga atttttaat 660
taataggaat ttattgggtt ttaagtttg ttagttttt tgtagtgttt aaatttgtt 720
ttttgtttg taaatttagt gtgtagaagg ttgttgggtt tttgggatta ttttttaa 780
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gtattttg tggtaggatt atagggtatt tgttgagggt agtttttgg gtagatttta 900
gtgtattgtg aagttagatt ttggttttgt gggttagtgg atgtgtattt tttattagat 960
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tggttttgt ataatgattt atttagtaat gtggttggtg atagtattat tatttatata 1560
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tttattatat aggattatgt ggattaaata agtttttgag gtttaatatg tggtatgaat 1860
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tgttgttgtt aagtttgtta tagttagtta gtggtggatt tgtttttaat atttatttag 2160
tagatatttt tttagtttgt atgtgattgg ggtttagatt taatttagtt tatagaggtg 2220
tatgt 2225

<210> 192
<211> 2205
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 192

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tttaaaagtt taagtatatt gtggagttga atgaaaaata gtttttgaa taattattat 120
taaatgagta aaagtttaaa aataatgtaa aaagttaaag ttggttgggt gtggtggttt 180
atgtttgtaa tttagtatt ttgggaggtt gaggtgggtg gattatgagg taaggagatt 240
gagattagtt tggttaatat ggtgaaattt tgtttttatt aaaaatataa aaattagtta 300
ggtgtggtgg tgagtgtttg gtggtgagtg tttgtaattt tagttatttg ggaggttgag 360
gtttgaaaat tgtttgaatt taggaggtgg gaggtgtag tgagtggaga ttgtattatt 420
gtattttagt ttggtgatat agtgagattt tgttttaaaa aaaaaaaaaa gttaaagttg 480
tttgagtaaa taaaagatta gataaaaatt ttatgaatta aaaattagtt ataaagttgt 540
ttaattagaa taggatgagg aagaaaaggg gaaattgatt atttttgatt aagtgtaaat 600
tttaagtaaa ttattgatat taatagtgag ttggagtatt ttgttttatt aggtaatttt 660
ttgtaaatat tttgtaatga ttttatatat ataaagtttt tttatgtttt tttttaaaaa 720
tatgagattt ttttaggtta atgtttaggt gagatgtttt ttgttgtttt agtagtttag 780
ttttattttt tttttggtt attatgaatg ttttttata attggagagt taggatgaat 840
taattttgag taagaaatgg gaaagtatag taaagaggtg atagttttgt atttttatat 900
ggaaaaagat ttagaggaga gtagtggtat ttttgtttta gttttaattt gaatggaggt 960
aggattttta ataatattgg atgttttttt tttttgttgt tttatgtttt tttgatgaag 1020
aagtaaaaag tggagagttt agttgttttt tagggttatg gagtttttta gttagggatt 1080
ttttttgtt atataattaa ggtttagggt tttgttttg tgattagttt tttggaagga 1140

gatggatggg ttttttagag atttttttag ggaggtggaa gtggggtttt gtatttagtt 1200
gatttgggag aaagaagtgg gatgatatga gggaggttgt tattaaaggt ggtggggtat 1260
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taattttaa atatgtttat ttgaatgtta gtatttttag ttttagaatt aatatttttg 2040
gttaattagt atttttgtta aatatatgat tgtgatttaa aataataaga aagtaatgat 2100
ttaatataat tttgatggtt attgatgtta aagattgttg ttgaaagttt taaatgggga 2160
gtgagtaatt ttaattttg aattggttgt tttgagttaa ggtta 2205

<210> 193
<211> 2205
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 193

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ttgttttaaa ttatggttat gtgtttggta agggtgttgg ttaattgaaa atgttggttt 180
tagagttaga agtattggta tttaaataaa tatatttggg ggttgggggt tgatgagtaa 240
ggttgggagg agataaaaga agtattttgg tttagttgtt agagatgtgt aaggtgtaat 300
ggagagagta atttaggttg tgagagtggt ttaaaatatt gagatatgga gttaggattt 360
ttgtttttgg gggatggttt tagtattgat gtgtaggatt tggtttttga aggagttgat 420
aaaattgttg tttatttgtg tgattattgg taaagtagtt ttatagtttg tttttttt 480
tggttgtttt tttatttatt ttttgttttg tttttttt tttttttt tttttttt 540
ttgtgtgaag tggaagtgat gtgaggtgta gtggaagtta ttgtagttgt ggtgttgtgt 600
tgtggggaag ggagaaggat ttgtaaattt tggagtgagg ttttgtttat ttgaggttgt 660
tgttgtgtgg agatttttgg gtgaagttat tgttattatg tttgattagg tattgggttg 720
ggagttattt aatggtggtg gttagggttt tttttgtagg tttgtttgtt gttaggttgg 780
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gtttttggag ttgtttgttt tttttgggt ttgtttatta ttttttgtatt ttattgtttt 960
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tgatttgttt attttggttt tttaaagtgt tgggattatg ggtgtgagtt attgtgttta 2040
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aaaattattt tttatttaat tttatgatgt atttgaattt ttaaatttaa tatatttatt 2160
tttttggttt ttaatttagt tttgtattat tttgtgagag taagt 2205

<210> 194
<211> 2355
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 194

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tgagttttat tgggttattt ttgtagagtt gtggttatat gttttgttag gtgttaggaa 180
gttatatata gtggtggtgt agatgggaga gggtatagta ggtattgtga ttatattgtt 240
tttagaggag tttgtgggtg ttttggattt tattgggatg aggtttgaga gttagttggt 300
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gttgtatttt tttatgtttg atattaattt ggttgaggtt ggttttaatt attatgttta 600
gaggattggg tagtttttt agggttttgg atgagatttg gttatggatt ttagtttatt 660
gaagtatttt tatagtttgg gttttgtgga tggatgttat ttagggtagg gtttgtagta 720
tggtttagtt atggatttgt gttattttat agattttttg gtttatttgt tttttatgtg 780
gtgttatagt ttagtgttga atatttattt agattatagg tatggtttat ggggagatgt 840
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gttgttgttg tttatagtta ttgtatgtgt agttgatggt atgatttatt tgattattaa 1200
tattttaatt gttgtaatat tgtttattat tatttagttt gttttagttt tgtggtttat 1260
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gttatgtttg tgggatgttt gtgagttaga gtttgggatt gagttttgtg tggttaggag 2340
gattgttgat agtag 2355

<210> 195
<211> 2355
<212> DNA
<213> Artificial Sequence

<220>

<223> chemically treated genomic DNA (Homo sapiens)

<400> 195

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ttttttgttt gtagtgatat gtttgaggta gagttgggga gattttggtg tagtataggt 180
ttatgaggtt gtttaagttt tttaggtttt gttatggtaa tgaaggttgt atgtgtaagg 240
gggggttaat attggttatt ttgggttaat ttagtagttg ttagggagg ttttggtta 300
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tgtttttgtt gtagtgtaaa ttgagtttgg tgttttttt gttgttgttg tagtatatgg 480
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aggttatatt tggta 2355

<210> 196
<211> 2380
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 196

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ataagattgt tttttaattt aatgatgaga ttataaatatg gtaataaaat gttttttttt 180
ggtttgggaa ttttttttg tggtataagg ttgtgtgatt ttaaattatt tttaatttat 240
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tgtgtgtgtg gattttaaat tttgaattta aatgaggggg agaaaattaa gttgattttt 360
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tattgtttat tattttttt ggttttgttt ttagttaaat ttttatagg tttttgttt 600
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<210> 197
<211> 2380
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 197

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ttgtattagt ttgttgttaa gtgtttagtg gtatatgttg tgaggggttg ttattatgga 120
tggtgtagat gttttatata tttagtattt taggatattt tgttagatgg tattgggttt 180
tgttttgttt gttgaggagg tggtttttta tttaggtttt gagtaggttt gagttgttgt 240
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gttggatagg tgaagagtga tttgttttg gatgatttta agaggtgggt tttttagag 540
aaattttgag ttttggtgta ggttattgtg ttttggagtat tgggggtgtg tgggttgtgt 600
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atgttatgt tttataaggg tattttgaat ttttaagtaa ataataattt tgaattagtt 2340
tttaattatt gatttttagt atagttatat gattagaaat 2380

<210> 198
<211> 2308
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 198

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gtatttgtgg ttggtttgat ttgtttttta ttttttgtt tgttttttt gtgttgggtg 180
ttgttgtgat atgttttgtg gatatttagg agtttttta gttttgtga gtgtggattt 240
gggagagagt ttttatttaa tgttgaggtt attggtttat agattttttt gggttatttt 300
gtgaagtgtt tggtttttt tatttttagt tttgtagtag taataaatgg gaaggaagtg 360
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tattgtggtg agattatatt gttataaa 2308

<210> 199
<211> 2308
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 199

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gatttttta tattggttgg gtttataggt ttgagttatt atgtttggtt agtttttta 120
atttaaaaaa tatagaaagt gttaatataa attaaaaagt tataaaatag tgttaatagt 180
attttatttt tttgaagata aatataggta gagaaaaatt aatggatatt gtttttttgg 240
gtaggggtat tattggttat tataattttt tttttgtgt attttagaat ttattaattt 300
ttttataaag attatgtagt ataataagat aataaatata attttgtgtg attttaaaat 360
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tgtttttgg gtttaagaga gtattttag ttaattttg tttttttagt agagataagg 660
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tattattagt tagttgtttt ttgtttgg 2308

<210> 200

<211> 2352
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 200

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gtttgtttat tattatttt gtaggttaat tttggttaga ggtggttatt tttggttttt 180
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ggagtttttt ttttttgt ttagttagat tgggatattt tatatataaa tatggtgtaa 660
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<210> 201
<211> 2352
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 201

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aaatgtttat ggtaaaaatg tgagttttaa ttgtagagtg gagttggtat tttttatatg 180
aggttttttt ttttaagggg atttgattg gatgggtagt atgagtgttt attttaatat 240
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taggagttgt tt 2352

<210> 202
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 202

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tatattatat taggtattga tgagtagttt ttttttttgt ttttgttgat tttggttttt 480
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ttttatagt 2229

<210> 203
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 203

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gtttgtggtt attattggga taaaagagaa gttagtttgg aggttagttt attgttgttt 240
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ggtttgttt 2229

<210> 204
<211> 2280
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 204

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aaaagtagga tattaaattt gttattttta gagggttttt tagtttttt ttttattttt 180
gaattgagtg aagtggtgtt gatttttatt ttttgggtat gagtttttgt gtatttggga 240
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<210> 205
<211> 2280
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 205

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<210> 206
<211> 2438
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 206

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<211> 2438
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 207

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<210> 208
<211> 2403
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 208

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<210> 209
<211> 2403
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 209

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<210> 210
<211> 2311
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 210

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<210> 211
<211> 2311
<212> DNA

<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 211

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ttttatttta ttttgtggat gtggttaagt tgtggttgta ggtggatgga ttgtggggtg 1560
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gtttattttg ttttttttt ttagggtttt tttttagaaa tttgggatat aaattggttt 1860
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gaggtagata ttttagtttt tttttgggat tttggttatg ttattgtgtt tttgttttgt 2160
aggttggttt ttggggggttt ttgatggtta attaaggggt tatttaggga ttttttaattt 2220
tatatatttt ttatttgggg gggtggtggg ttatttttt ggtttgtgtt agggatagag 2280
gaaaatttgg tgtgtttttt ggtgttatag a 2311

<210> 212
<211> 2271
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 212

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gtggtagggt tggggtgagg atttagggat ttgttatttg tgaggtgttt ttgtatgtta 180
tattgttttt ttaagaatgt gtatagtttt agagtttgaa ggtttaaaat atagggtata 240
gggatattta aagagtgatt tgttttttt agtttttgta ttggtaggag tttggaagga 300

taattttga gttttttt ttaaaattag agttttgaa tttgataatt tgattttaag 360
gatgttgata gtaggtgtta tgtttgatgt ataatgaata ataaagtatt tatttgtgtg 420
ttaggtgtgg tttgtatgt tttgtatgta ttaatttt gagttttata ataaatttta 480
ttagatgggt atgataattt atatttttat tttttaaat gagaaaattg aggtttagag 540
aggttaagta aattgtttaa ggttgtagag ttgggaagta gggaagttag gatttgtatg 600
taggagtttg tatttagagg ttgtgggtta attattgaat agtattgttt ttttgaaggt 660
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gaagttagga ttgttattaa gtttattttt agatgaggaa atagttgttt agagaggtta 2160
aggtatttgt tttaaattat atagtagtta gtattggtgg tagaatttaa atttagattt 2220
gtttggttgt aaaaatagtt attgtttagg aggtattttt tgttttttt a 2271

<210> 213
<211> 2271
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 213

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tttgaatttt gttattagtg ttaattattg tgtgatttgg ggtaagtgtt ttgatttttt 120
tggatagttg tttttttatt tggaaatggg tttggtaata gttttggttt ttaaagttgg 180
tagtgttttt ttagtaagta agttgtgtga aatggtggaa ttttggtttt ggtgtagaga 240
agggtatgat gattgtgtta gggtttgttt ttttggaat tttttttgg gaatggtaga 300
gggtagtggg gtgttttgag gtaggttgtt gttttgtttt tattttttt ttttagttgt 360
tttgttttag ttgtgatgat tttgtttttg tttgtttaag gggtaggaag gaagtgagga 420
gggtagttag tagttttttt tttttgttt tgttttaggt attaggtttt tttttttta 480
gtgttttaga ggaggggatg gtagtattat ggattttgt ttgtttattg tttgttagat 540
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gagaagtggg gattttttt ttgtgtttt agtggggagg taggggttgt gtttttttag 1140
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gagtgtttta ttatttgttg tgtattagat atggtatttg ttgttagtat ttttggagtt 1920
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gtatgggttt agataagttt tttttgggt tttagttttt ttttataaa gttaggggta 2220
aggtgatgtt gattggttta gaggttttta attttgatgt ttttagggtt t 2271

<210> 214
<211> 2546
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 214

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gtgagtatta attggatgtt tgtaaagtgt tagaggtagt ttgtttttga attagtattt 180
tttttaagat tggatttatt ttttgttatg tgtggggagg aaatttttga attattgaag 240
ttagtggttg agtttatatt attttagtta gtttatagtg gttatatttt tgttaagttt 300
gttgatgggt agttttattg gagtgtagat gttatttttt taggaaattt gtgatgagga 360
ttggggtgta tatgtgtgtt gaggatattt tttaaggttg gttttggggt ttagataggt 420
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atggttgagt gtgtggtttt gaattttatt tttggaatag aggaagtttt tgttatgaga 540
aagaatttta gttatagtgg atttgtattt gtaggtttgt gttttgtgat atttaagggt 600
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ggtgggtttg gttatggtgg ttttgggtgt ggtgggtttg ggtgtggtgg ttttgagga 2460
ggagtgtgtt ttggagaata ggtgggtgtg tgagagtttt tagtttagtt ataagagtaa 2520
tatatgttgt ttatttagtt ttgttt 2546

<210> 215
<211> 2546
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 215

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ttgaggttat tatggttggg tttattatgt ttaggtttat tatatttagg gttattatat 180
ttgaggttat tatgttagaa gtttattatg tttgggttta ttatatttaa ggttattata 240
gttgaggttt attatgtttg aagtttatta tgtttgggtt tattatattt gaggttatta 300
tgtttgaagt ttattatgtt tagggttatt atatttgagg ttattatgtt tgaggtttat 360
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gttagttgtg atatgtttta tatgaggagg aaggttttag tagggtttag tatagatgtt 480
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aattaggttt gaaggttggg agatgttttt tttgttatat ggagagttta gttttttggt 600
tatttttgg tggttaatat atttttaggt agataaggga atttgttagt tattggggtt 660
ataaattttt ttttagggt tagagtttgg taatagggat agttttagtt tttatttttt 720
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ttatagtttt agggttaggg tttggttttt tagggtttgt gtaaggggtt tgtttttatt 2520
tttaggtttg gtttttgttg gggttg 2546

<210> 216
<211> 2251
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 216

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agttgtttgt gttgtttgtg gttggggtgg agggtagtta gagttgggga ttaaggtttt 120
gtgttatttg tgtgtatagt tttatatttg aatgttgttt ttttgtagat gagattggtg 180
ggtattgtaa agttgggatt tgtttttgaa ggaaaaaaaa tagtgagtaa gaaatttagt 240
attatttttt attgatttat tttgttgtat tttttgtttt ttaagttttt gaaagttggt 300
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gatggtgttg ggttgatgtt ggggttaatg ggtagagaat gtagggatgt ggtttttgtt 540
gaagagagtt aagaagggaa gagtgtgttt tttaaattgt ttttgtaatt tgtttttagt 600
gagtatttta ttgatttaga atttattgag aatagtatta gtgagttatt tttttttga 660
gatgggtttt atttattttg gtaatggagt gagttggatt gtggggagga agaggaatgg 720
gaaaattagt ttataaatat taatgttagt aagagtgtgt tgttggtagg atgtattgtg 780
agtttggaga ttttggtggt tgtagttggt aagtggttat aatttagaaa gtaggattga 840
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tatttttttg tattgtgaat tgtgaattgt a 2251

<210> 217
<211> 2251
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 217

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aggggtaagg gttgttttgg tggagaaaga aatttaggtt tttgggaata taaattgggg 180
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<211> 2413
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 218

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<210> 219
<211> 2413
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 219

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<210> 220
<211> 2222
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 220

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aaaaaaaaaa aaaaaaatata tattatataa ttggtaaatt tattaattta ggtttattta 600
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tt 2222

<210> 221
<211> 2222
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 221

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ag 2222

<210> 222
<211> 2162
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 222

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gttgaatgtt aggatatggg taggaggaga gggttggagt tgaattgtgt ttaagattgg 2100
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<210> 223
<211> 2162
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 223

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<210> 224
<211> 2586
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 224

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ttaagtaggg tagttttagg ttaaaggtat tttagaataa taagattatt ttaagaaatg 240
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tggggt 2586

<210> 225
<211> 2586
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 225

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gggttatttg tagtatttg tggttaagga ttgtgtgtag atttgtggag ttgatgtgtt 180
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gaatattttg agaaaagagg ttttagagaa ggtaggagtt tgtttttgtg aaatattaat 300
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tgtggg 2586

<210> 226
<211> 2257
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 226

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gtgttttggg tatattttga tagtgatata gttgttttga tagggttgtg gtttttttg 180
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tgttgtggtt ttatttagtt tttgttggtg tggtttgatt ttttaaatgtg tgttagtaag 300
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ggtagtaggt gttaaattag tattagtgtg gatttag 2257

<210> 227
<211> 2257
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 227

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<210> 228
<211> 2352
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 228

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ttttgtttt agtttttga gtagttggga ttatagttat gtgttattat gtttggttaa 2340
ttttatatt tt 2352

<210> 229
<211> 2352
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 229

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attgtatttt tttttgggtg atagagagag atgttgttta ttttgtttt tattaaaata 180
aataaataaa taaataaaaa aaattttgag attgggtaat ttatagagaa aagagtttga 240
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gtgtttaggg atgatatgtt ttatgggggg atttgtttt taggggttag ggtgtttggg 660
aagaggttgg gagttggtgt ggttgtggtt ttttatttta ggtattatag attagggttg 720

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gtagtagggg tg 2352

<210> 230
<211> 2470
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 230

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ttttaaaatt tggggaaaat ttttaaattg gagaaaaaaa tttaatatta gtatttatta 180
tataaagtat taaaaatatt ttttagtagt tttgtttaag tattttaggt tagtggtagt 240
atgttagtta aaatgtaatt taaaatgaat gaataatagt tagttggtag atattgtatg 300
taatataata tggaaatata ttggaagtat tttaaaattt aatatttgaa tttgtgaatg 360
tttaaattaa gtattttaaa ttaggtgttt attttgaaa taatatttta aaatatgtgt 420
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aaaaaggttg atgtttagaa gtgttggttt tttttatttt gtgtatttga gaggttatgg 660
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aggagggtgt ttgtggtggt tttggtgtgg agtttttttt tttttttttg taggattttg 840
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ttttaaataa taataaaaat tttattatta tttatttaaa aggtttttgt gttgtggtta 2460
gatagtgatg 2470

<210> 231
<211> 2470
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 231

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ttattgtaat ttttgttttt tgggtttaag tgattttttt attttatttt tttgaggagt 180
tgggattgta ggtgtgtgtt attatggttg gttaatttta tttttgtag aaatgagatt 240
ttaatatgtt gtttaagttg gttttgaatt gttgagttta agtgatttgt tagttttggt 300
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tgatttttta ttttataggt tgtattttag gtgggtagtg tagttaggtg aatatttaat 540
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ttttgtgtaa aatttttttt gtttagtttt tttaaagttt tttttattgt ttttgtgat 660
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ggttggtttt 2470

<210> 232
<211> 2305
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 232

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gaataaaatg tgaattttag ttaataatag tgtaaaatat tggtttatta attgtaataa 180
atgtattata ttagtatgag atgttaataa taggggaaat tggatgttgg gtatatggta 240
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ataaaataat ggttatttat atatttaata tttggtttaa taatggttaa tatagttaaa 360
gtttttttt attgtttttt ttttattaga tatgattgtt tttttaatt tgatttttat 420
tttttgtat ttttgattt ttttaattat atatgtatgt ataattaagt aatatatagt 480
attgttttat aagttttaga gttgaatgta tatgaattgt tatattattt atttttttat 540
atttttttt ttttgtttta ttatattttt gagtttagtt tttttttatt ggtgtataat 600
attatatttt aatattttat aaggtattta ttttgttatt gatggatgtt tttaattttt 660
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ggatttagtg gaggattatg ggttt 2305

<210> 233

<211> 2305
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 233

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ttttatatat ttaaaattga aggtattttt taaaatgatg ttttatagtt tgtaagagta 120
ttaaaattat ggtaattagg atttattata aagagtaatt tgtagtttgt ttgattttgt 180
tgatgtttat aaattagata aaatgatgaa ttatggttaa atgttttttt ttatttaaag 240
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ttttaaaata ttttttttt gtttgattat tatgtggggt taaaatttta aaaatagttg 360
gaaattgttt tatgtattaa ttaagggtag tgagggttta ttatttagga tgattttggg 420
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aagatttgga ataaaaaagt tatattgaaa ggagttagaa aggtattagg ttatgtggtt 600
tttatatagt ttatgtgaga ggggttattt atagtattgg agatgtagtt atgggaatat 660
aaaatgaagt tttttaaaga ttaatttgag ttgttttatt ttaagtgatt tagttttgtt 720
tttttgtaa atgttttttt gtagggttgt aatattgtag tttggttttt agtttatggt 780
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gttaatggat tttaaatagg ttagagagtt tttttatggt tttaatgaat gatttttgag 900
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taaagaagtt aagaaatata agagaatgaa aattaagttg agaaaagtag ttatatttgg 1920
taaggagggg ataataaagg gaggttttaa ttgtattgat tattattaaa ttgggtgtta 1980
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aatattttat gttaatatgg tatatttgtt gtaattaatg aattaatatt ttatattgtt 2160
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ttttgtggtt gtggtagttt tttaa 2305

<210> 234
<211> 2234
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 234

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<210> 235
<211> 2234
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 235

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<210> 236
<211> 2317
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 236

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<210> 237
<211> 2317
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 237

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<210> 238

<211> 2553
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 238

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<210> 239
<211> 2553
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 239

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<210> 240
<211> 2381
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 240

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<210> 241
<211> 2381
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 241

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<210> 242
<211> 2514
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 242

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taggggatgg taggaattta tttgatttt ttttggggtt tttgggtagt ttttttattt 2460
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<210> 243
<211> 2514
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 243

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tattttttag gagttttttt gtaaagggtt aggtagggtt tgttgatatg tagagaatgg 180
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<210> 244
<211> 2325
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 244

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tggtggattt gtggagattt tattgtttta ttatgggtag ggtggggttt tggggtattt 180
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aaaataaaaa gttagggata ggaagtattt tgtttaaaga tttat 2325

<210> 245
<211> 2325
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 245

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<210> 246
<211> 2541
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 246

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<210> 247
<211> 2541
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 247

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<210> 248
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 248

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<210> 249
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 249

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ataattattg ataattttta agaaatatag atattaaaat attattttta tttttttaat 420
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<211> 2257
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 250

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<211> 2257
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 251

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<211> 2434
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<220>
<221> unsure
<222> (1598, 1841, 1846, 1848, 1869, 1871, 1873, 1874, 1878, 1880)
<223> unknown base

<400> 252

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<211> 2434
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<220>
<221> unsure
<222> (555, 557, 561, 562, 564, 566, 587, 589, 594, 837)
<223> unknown base

<400> 253

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<211> 2476
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 254

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<211> 2476
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 255

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gtgtttttgg ttttttgggt tttggttgag tttgtttgt gttgagtttg tggttggagt 2340
tttgtttgta ttgggggatgg gttttgtgtt tgggatgttt aggttgggtg tttggtgtgg 2400
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tgttggtttg gggtta 2476

<210> 256
<211> 2520
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 256

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ggggtgtgag gagatttgtt ttgtttagtg ttgggtatga tgtttatttt tgtttgaaga 180
tttggaatga gttttttttt tttaattgtg aaatgggagt ggtgtaagtt tttagttttt 240
tatttgtgat ttttaagttt taaagttgtt tggaagttta gaagtttttt gtaatttaat 300
tggtggtaaa attgtgtttg aattgatgtg aggttgttga tggtttttat ttgttaaatt 360
tgtgtgaata tttatgtttt gttgtagaaa tgtaaatgag tttgatgatt ggttgttgtt 420
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aagtttagt tgttttgtat tttgaagtgt atttgggtat ggaatggggg attgtgggtt 540
tgttgttggt ttaatagttt tgttagttt ttaggagttt ggggttagat gagagggtgg 600
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aattgttttt ttaaaagatt atgtgttttt aaatttatgt ttaatgagtt gattatttta 2460
tgagggtgtt aggtgatata gtgaagatta tatatgtata gagtgataga atgttggtag 2520

<210> 257
<211> 2520
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 257

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tatttttata gaatttggtg attttaaata ttaaagttta ttagttagtt gtaaaaattt 180
aattaatagt ttatttatgt gatagtgttt tggaagtttt tattattttt tttttggttt 240
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agaattgaat taagattttt tttttaagag agagaatttt gttttgttat ttaggttgga 360
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ggttatatag tgaattaggg ttataagtgg ggttaaggag tagtttgttt ttggttaatg 480
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ggttttgtgt gggtgtggtt tttagtgtgt tatttttgtt ttttgttttt tttttgtggt 2460
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<210> 258

<211> 2555
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 258

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tttttttttt ttttttgtag gaagttttat tatttaaaat tgtttgttta ataattatta 240
ttaagatgtt atttttgagg gagtatatat agtaggtgtt taataaatat ttaataaatg 300
aaggtatttt ttgaatgatt tatttattta gtaaggagtt tttgggtatt tattttgtat 360
taggtattta attaggtttt ggagagagga aatttaagga gtttaggttt aatgagattg 420
atgtatatgt tagttattta ataaaaagtg gtgtgtgtag tggaagaagg tgtttgggag 480
taaagaggag gtagttttta ttttagttga gttttttagt taaggggttg gggtttgtaa 540
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gatttaatat tatagttttt ttttaggttt tgataatagt tttttttttt tgtttttgaa 2460
aatttttttg tttatttttt agtttattaa tttttggttt attgttagtt attttttggg 2520
ttgagtattt gggttgtagt tataaatagg atttg 2555

<210> 259
<211> 2555
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 259

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tattaaaatt tagaaagaag ttatagtatt aagtttggat gttttagta tagagagagg 180
aattgaatta aagatatttt aagatttatt gatatattta agaaaatatg ttatagaggt 240
ggtattttat ggatgggtgg gaagggattt ggttttttt agtgaggttt ttaaggagtt 300
agtttaggga gggtggggtt gttttatgt agaggagttt taggtttagt atagggtttt 360
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gtgggttgtt taggttttta gtttattttt gtttt 2555

<210> 260
<211> 2516
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 260

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ggaaatattt ttttgaaaa ttagtataag ataagggtgt tttttttat tatttttatt 360
taatatagta ttgtaagttt tggttagggt aattaagaaa gaataaaatg aagggtattt 420

aaataggaag agaggaagtt aaattatttt tgtttgtaga tgatgtgatt ttgtatttag 480
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<210> 261
<211> 2516
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 261

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aaaatataaa tataaattag taaaaaataa atttataaaa tgttaggttt ggagttgtaa 180
taagatagag ataggagtag tatatatgtg gtttaggtgg ggaggatggg tgtaaatatt 240
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atgttggttg tttgggtttt atgtttggta tgaagaagtg taggtagggg aagggtattt 960

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<210> 262
<211> 2364
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 262

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gtttttatgg tagggtaaga gtttttatt ttttgttgg tttttgttt tgttttgaga 240
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atattgataa tttggttata aaattttaaa aatttttgtg tatttataaa taaaaaaaat 600
tgaaaagtta tagaatggaa gatatttata tttttgtat attgtttttt aaaaatgtat 660
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tttgtgggaa attttttta tttt 2364

<210> 263
<211> 2364
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 263

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gagttaattt ttttgttttg tattggaagt gaattgattg tatatatagt ttttgttata 180
tatatatgtt tttttgaaa gtattagttg tgtaaagagt ttagaaatgt ataggagaga 240
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gaaagtggta ggaggagagg agttgtttgt ttagttgggg tggagttgat ggtttgagga 720
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aaattttgt ttgttatgg aaattatttt gtaaattttt gatgtttgta ttttagttta 2220
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gttgtttggt agtgttagtt ttgt 2364

<210> 264
<211> 2408
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 264

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agaggttgat atagtttagt tttggggttt ggttttattt ataagaggtt atattttgtt 180
atagtattgt ttatttggtt tgttttagaa gtattgttag agtggtgaag gtaggaggtg 240
gtgtatgaga gtttatgttt tagtatttat ttaagtgagg gaaaggtgtt ttgtatttag 300
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gatagtggat ttagagttat gttgtggttt ttatttgttg ggagttagta gtgtttgtgt 420
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gatttaggga gttaagagtg tgagtatttt taggttttaa tttgttgaat gttgtgtatt 720
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ggggagtg 2408

<210> 265
<211> 2408
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 265

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agggagagtg tttattgttt ttagtagttg ttatttttt tatgattaaa gtgggaggag 180
agtggtattt ttgtatagat tattttgaa gtgaggggta gattttaaga gtttttaga 240
gtttgagttt tgggtttgtt attgtggggt ttaatgtata attagggttt tttgaaaatt 300
tttgtaatgg ggatttgtta tggaaatttt tatagatttt ggttaatttt ggaatatatt 360
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ttatgtgt 2408

<210> 266
<211> 2523
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 266

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gtagttggga ttataggtgt ttattattat gttttgttaa tttttgtat ttttagtaga 300

tatggggttt tatttgttg gttaggttgg ttttaaattt ttgattttaa gtgatttgtt 360
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tta 2523

<210> 267
<211> 2523
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 267

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ttgttagtta tttgtggtgt ttttgggttg tttttttta gttttgttt ttgatgttat 180
gtgtttgatt tttttgtt gttagtagtt ttttataag gtgttggttg ttgtttttgg 240
gattttttt gtttgatttt attttaattt gattatttat aaagatttta tttttagtgt 300
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gag 2523

<210> 268
<211> 2280
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 268

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atatgagttg ttagggaaat gtttgttttt gtgtgtgttg tatgtgtagt ttttgggta 240
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tgtttaattt aggagtggag aaggaagtta gaggattttt tggaggtggt aggtttaatg 2160
ttttgtttt ttatttattt atttatttat ttatttattt atttattttg taattaattg 2220
aaagaaggta gaaggagttg atgggttttt taggttggaa attttataag tattaggatt 2280

<210> 269
<211> 2280
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 269

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tattaaattt gttattttta gagggttttt tagttttttt ttttattttt gaattgagtg 180
aagtggtgtt gatttttatt ttttgggtat gagtttttgt gtatttggga gatttttgaa 240
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ggttttgtaa aggatgtatt ttttgagttt ttttttgta tgtttagtgg ggtttgtttt 360
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tagggtaagg gtttgtgtat ttttaaagat aagtggggtt tttggaaggt ttttaggtag 660
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atttgtgat ggaaagttta tgttgatttt gtttggtatt taaggtgtgg gtagtggttt 2220
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<210> 270
<211> 2413
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 270

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ttttaaggtt ttaaagttag tttgtttttt tagaggtggg gggaagtagt tgtgtttttt 180
attttaggat atatatgtat ttatttttta taatatatag gtagatatat atttagtttt 240
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aattgataag ttt 2413

<210> 271
<211> 2413
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 271

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tgggaggatt tttttatt tagagttgat atttttag gggttttt ttatttagag 180
ttgatatttt tttaagggtt ttgtttatt tagaggtgat atttttag gggtttttgt 240
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atggggtggg tag 2413

<210> 272
<211> 2171
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 272

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gtaatagagg aatatttttt gttttatgtt tattttattt tgtaattttt taaggttttt 180
ttttttttt ttagaatttt aaagtgtatt tgaatttata ggtaaaattt ttttagaatt 240
ttgtgagaat ataaatgatt tgattagttt ggtattgttt ttggggattt gggaaaattt 300

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<210> 273
<211> 2171
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 273

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<210> 274
<211> 2490
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 274

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<210> 275
<211> 2490
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 275

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<210> 276
<211> 2418
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 276

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<210> 277
<211> 2418
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 277

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<210> 278
<211> 2351
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 278

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agttgttttg tggttgtagg ttttgtgttt tgtgtattag ggaaaagtag ttttgagtt 180
tgtgttggat gttttgtgt tttgttattg gttgttttg gtttttgggt gaggtgtttt 240
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tgtattgtgg gtttgtttag agttgggatt attgggttgt gtgtgggttg ttaggttagg 480
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tttttgggg a 2351

<210> 279
<211> 2351
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 279

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atatagttta ttgttgtggg gtattaagtt ttggtggtta gttttgtatt ttatttttt 180
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gaggttggtt t 2351

<210> 280
<211> 2427
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 280

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tttttgggg taggaggggt tattttggta gggtaaaaag agataaatag aaaaataata 180
gtaataataa tagtaataat ttggggttgt tgttatgggg tttgttttga ataggttgtg 240
tttagtttat tgtgaggaag gatgtttagt taggttttgg ttgaagtttg tagttgggtt 300
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ataggtgagt gtggttagtg agtggag 2427

<210> 281
<211> 2427
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 281

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<210> 282
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 282

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<210> 283
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 283

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<211> 3190
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 284

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<211> 3190
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 285

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<210> 286
<211> 2613
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 286

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<211> 2613
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 287

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<210> 288
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 288

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<210> 289
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 289

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<210> 290
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 290

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<210> 291
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 291

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<210> 292
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 292

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<210> 293
<211> 2501
<212> DNA
<213> Artificial Sequence

<220>
<223> chemically treated genomic DNA (Homo sapiens)

<400> 293

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ttgtatttg gttttttta ttttgttgtt gtagggtggg agggggttgg tgtgggttga 5340
tgtttgtagt ttttatttt tggattattt tttttagggt ttgggagttg tgtagtttta 5400
gatttttgg ttaaggattg gtttgggtgt tttgaaagtt tgtaggattg agttgttagt 5460
tttttgtgga gtgggtgtt tataagttag ttttttggt atttattttt tgtgtgtaaa 5520
tttggttgtg agtttttttt gaaggtagaa gtggttggta tggattgttt ttaaggaagt 5580
ttagttttag gtttagttat ttgggttttt tttgtttgtt tagggatgtt gtgagggaag 5640
tgattgtgtg gattgtttgt tattagttgt tttttaaatg tgtgtagaat ggaggtgaaa 5700
ggttggtttt ttttttttt tttgtttggg ggtttggaag aaggtaggat tttatgagga 5760
tattttttgt tagtttttta gtgggtttgt gaatgtttat gttgagaggg gtgtagatgg 5820
ggttaggtgt ggaggaaaga agggtttgtg gtgttgtaag gtggaggaag tagaggtttg 5880
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tcaatcccta aaacccaaa 19

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ggaagggaag gatgagagta t 21

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<220>
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<400> 299

acccaaacta acaatcaaaa at 22

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caaaataacc aatcccctaa a 21

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<220>
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<400> 302

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<400> 303

ccccaatata aatctaccaa cc 22

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<400> 304

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cctccaaaat cttaaccaaa t 21

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<400> 306

tttattttag gagggaagga tt 22

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cccaactaac tcaaattcca c 21

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<220>
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<400> 308

gtggttttgg ggaattagta t 21

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<400> 309

ctcctacata tcccatctca tc 22

<210> 310
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<220>
<223> Detection primer for UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN)

<400> 310

aattaaggtt tagggttttg ttt 23

<210> 311
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for UBIQUITIN-LIKE PROTEIN SMT3C PRECURSOR (UBIQUITIN-HOMOLOGY DOMAIN PROTEIN PIC1) (UBIQUITIN-LIKE PROTEIN UBL1) (UBIQUITIN-RELATED PROTEIN SUMO-1) (GAP MODIFYING PROTEIN 1) (GMP1) (SENTRIN)

<400> 311

accttcccta caaatctacc tac 23

<210> 312
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN

<400> 312

atagttttgt gggtttaaga gg 22

<210> 313
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN

<400> 313

accctaacct tatacaatac caac 24

<210> 314
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN

<400> 314

ggtggggtta ttaaggagtt ta 22

<210> 315
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for BASSOON; ZINC FINGER PROTEIN 231; NEURONAL DOUBLE ZINC FINGER PROTEIN

<400> 315

ctcaactacc atacccaaaa a 21

<210> 316
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<220>
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<400> 316

ttgtgttggt tgtaaaagga 20

<210> 317
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<220>
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<400> 317

caaacactat acacctctca aca 23

<210> 318
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<220>
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<400> 318

ttgaggttat tggtttatag atttt 25

<210> 319
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<220>
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<400> 319

ccctaaccac cccttcta 18

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<220>
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<400> 320

tgtgtgaaat gttttagttt aattg 25

<210> 321
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<400> 321

actccataca cttttaccaa cc 22

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<400> 322

tgtgttagga atgattgggt a 21

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<220>
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<400> 323

aatttcaaaa ccaaaatcac c 21

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ggttgggatt ttagtgtgtg 20

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<400> 325

aattaccaaa ccaattcctc tta 23

<210> 326
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<400> 326

ttatttgagg gatttattgg ag 22

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ccttattaaa acttaccacc ctat 24

<210> 328
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gtgggttagt gggaggttat 20

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taaaaaccct tcctacctct ta 22

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<400> 330

agatgggtat gtattttggg tt 22

<210> 331
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<400> 331

actaaactca accacctcac taa 23

<210> 332
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<220>
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<400> 332

ttttggttag ttttatgggg ta 22

<210> 333
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<220>
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<400> 333

cactacttca aatccatcat ca 22

<210> 334
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for LYSOSOMAL-ASSOCIATED MULTITRANSMEMBRANE PROTEIN (RETINOIC ACID- INDUCIBLE E3 PROTEIN) (HA1520) LAM5

<400> 334

aagagtgagg agtaagggag tt 22

<210> 335
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<212> DNA
<213> Artificial Sequence

<220>
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<400> 335

taacttcaca aattacccaa ca 22

<210> 336
<211> 22
<212> DNA
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<220>
<223> Detection primer for "TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE)

<400> 336

ttttggggtt agtatgtgag tt 22

<210> 337
<211> 20
<212> DNA
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<220>
<223> Detection primer for "TYPE I INOSITOL-1,4,5-TRISPHOSPHATE 5-PHOSPHATASE (EC 3.1.3.56) (5PTASE)

<400> 337

atcccaacaa cttcttcctc 20

<210> 338
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE)

<400> 338

gaagaggaat gggaaaatta g 21

<210> 339
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE)

<400> 339

tcaccaacaa aatacccaa 19

<210> 340
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE)

<400> 340

tgagtaagat gattatttgg attt 24

<210> 341
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for PROSTAGLANDIN E2 RECEPTOR, EP4 SUBTYPE (PROSTANOID EP4 RECEPTOR) (PGE RECEPTOR, EP4 SUBTYPE)

<400> 341

aaccatcaac catacctatt tc 22

<210> 342
<211> 22
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<220>
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<400> 342

attgggtttg aaagagttgt ag 22

<210> 343
<211> 21
<212> DNA
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<220>
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<400> 343

cacttcccac ctccttatat c 21

<210> 344
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<212> DNA
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<220>
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<400> 344

atgatgggaa tatgtaagaa tga 23

<210> 345
<211> 24
<212> DNA
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<220>
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<400> 345

cttctcacta ctaatctcct accc 24

<210> 346
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for EQUILIBRATIVE NUCLEOSIDE TRANSPORTER 1 (EQUILIBRATIVE NITROBENZYLMERCAPTOPURINE RIBOSIDE-SENSITIVE NUCLEOSIDE TRANSPORTER) (EQUILIBRATIVE NBMPR-SENSITIVE NUCLEOSIDE TRANSPORTER) (NUCLEOSIDE TRANSPORTER, ES-TYPE

<400> 346

gagttggagg gttttgtttt a 21

<210> 347
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for EQUILIBRATIVE NUCLEOSIDE TRANSPORTER 1 (EQUILIBRATIVE NITROBENZYLMERCAPTOPURINE RIBOSIDE-SENSITIVE NUCLEOSIDE TRANSPORTER) (EQUILIBRATIVE NBMPR-SENSITIVE NUCLEOSIDE

TRANSPORTER) (NUCLEOSIDE TRANSPORTER, ES-TYPE

<400> 347

caaactccca taaaattcat ct 22

<210> 348
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR)

<400> 348

gtgtgaggtt tgggtatttt t 21

<210> 349
<211> 19
<212> DNA
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<220>
<223> Detection primer for ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR)

<400> 349

ccactcactc aacccataa 19

<210> 350
<211> 22
<212> DNA
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<220>
<223> Detection primer for PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN)

<400> 350

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<210> 351
<211> 24
<212> DNA
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<220>
<223> Detection primer for PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN)

<400> 351

aaaacctatc tacacctttc tctt 24

<210> 352
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<212> DNA
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<220>
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<400> 352

aattagagaa ggttaaatgg gtt 23

<210> 353
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<212> DNA
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<220>
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<400> 353

attcccacca aaacctctac 20

<210> 354
<211> 20
<212> DNA
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<220>
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<400> 354

gggatttggg aatttattgt 20

<210> 355
<211> 21
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<220>
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<400> 355

aataactcca actttcctcc c 21

<210> 356
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<212> DNA
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<220>
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<400> 356

ggtggatgag tagtttgaag ttt 23

<210> 357
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<220>
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<400> 357

aaaaacccct ttccctct 18

<210> 358
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<220>
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<400> 358

gttggggttt agtaattgaa aa 22

<210> 359
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<212> DNA
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<220>
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<400> 359

accaacacaa actaacactt acat 24

<210> 360
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN)

<400> 360

aagaggtttt atggtgtttg ag 22

<210> 361
<211> 21
<212> DNA
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<220>
<223> Detection primer for PEROXISOMAL MEMBRANE PROTEIN PEX14 (PEROXIN-14) (PEROXISOMAL MEMBRANE ANCHOR PROTEIN PEX14) (PTS1 RECEPTOR DOCKING PROTEIN)

<400> 361

cactcccttc ccaaactata c 21

<210> 362
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2)

<400> 362

gtggaaaaag gagagtaaat tg 22

<210> 363
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for HOMEOBOX PROTEIN HOX-B6 (HOX-2B) (HOX-2.2)

<400> 363

ctcctcaatt ctcaccaaaa 20

<210> 364
<211> 20
<212> DNA
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<220>
<223> Detection primer for LIM DOMAIN KINASE 1 (EC 2.7.1.37) (LIMK-1)

<400> 364

agggaggttt ggtgtatttt 20

<210> 365
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for LIM DOMAIN KINASE 1 (EC 2.7.1.37) (LIMK-1)

<400> 365

aaaccctact tcctacaaac aa 22

<210> 366
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32)

<400> 366

ggaaaggata ggatgttgga t 21

<210> 367
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32)

<400> 367

caatcccctt aaaacaaacc 20

<210> 368
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for 1-ACYL-SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE GAMMA (EC 2.3.1.51) (1- AGP ACYLTRANSFERASE 3) (1-AGPAT 3) (LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-GAMMA) (LPAAT-GAMMA) (1-ACYLGLYCEROL-3-PHOSPHATE O- ACYLTRANSFERASE 3)

<400> 368

ttagggagat gagattaaag ga 22

<210> 369
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for 1-ACYL-SN-GLYCEROL-3-PHOSPHATE ACYLTRANSFERASE GAMMA (EC 2.3.1.51) (1- AGP ACYLTRANSFERASE 3) (1-AGPAT 3) (LYSOPHOSPHATIDIC ACID ACYLTRANSFERASE-GAMMA) (LPAAT-GAMMA) (1-ACYLGLYCEROL-3-PHOSPHATE O- ACYLTRANSFERASE 3)

<400> 369

cacaatttcc cacaaaaca 19

<210> 370
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for HOMEOBOX PROTEIN GSH-2

<400> 370

tatatggggt gggagtattt t 21

<210> 371
<211> 21
<212> DNA
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<220>
<223> Detection primer for HOMEOBOX PROTEIN GSH-2

<400> 371

ccttccccte cttcttatac t 21

<210> 372
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
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<400> 372

ttaggggtta ttaggttaaa tga 23

<210> 373
<211> 23
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<220>
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<400> 373

aaaattcttt cctctcctaa aca 23

<210> 374
<211> 20
<212> DNA
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<220>
<223> Detection primer for HISTONE H4

<400> 374

ttagttgaga aagtgggggt 20

<210> 375
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for HISTONE H4

<400> 375

ctacctcaaa ccaaaatcct c 21

<210> 376
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2)

<400> 376

ttttggagtt atagggtttt gt 22

<210> 377
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2)

<400> 377

cttcaacatc tcccaatcc 19

<210> 378
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22)

<400> 378

gggttatgtt aagggagaaa g 21

<210> 379
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT

OF AP-1 CLATHRIN) (DC22)

<400> 379

aaacctaaaa atccaacaca aa 22

<210> 380
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for

<400> 380

atttgtggta gttaataggt atgttta 27

<210> 381
<211> 21
<212> DNA
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<220>
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<400> 381

aataacctaa tctccaaacc c 21

<210> 382
<211> 22
<212> DNA
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<220>
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<400> 382

tagagaagtt gtttgttggt tg 22

<210> 383
<211> 24
<212> DNA
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<220>
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<400> 383

tacccaccat ataccaaaac taaa 24

<210> 384
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for PERIPLAKIN (195 KDA CORNIFIED ENVELOPE

PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)

<400> 384

attgagggg tattatttgt tg 22

<210> 385
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)

<400> 385

aaccaccttc tcccctaat 19

<210> 386
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection primer for

<400> 386

gtaataattg ggttaggggt ta 22

<210> 387
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
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<400> 387

aaccaatatc aaataactaa aatcc 25

<210> 388
<211> 22
<212> DNA
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atttttgttt atggtagtt 19

<210> 614
<211> 16
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<220>
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<400> 614

tgcgtatcgt tagtta 16

<210> 615
<211> 17
<212> DNA
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<220>
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aggttgtgta ttgttag 17

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<400> 616

attcggcgaa tagtag 16

<210> 617
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<220>
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<400> 617

tatttggtga atagtagta 19

<210> 618
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<400> 618

atagcgttgg tcgtta 16

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<400> 620

ttcgggatac gagttt 16

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tacgataagt cggaga 16

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<400> 623

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<400> 624

tatcggcgag ttgtat 16

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<400> 625

ggttattggt gagttg 16

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<400> 626

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ttaatgtttg gggatgt 17

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<400> 628

tattcgcgtt tttagat 17

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<220>
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<400> 629

ttatttgtgt ttttagatta 20

<210> 630
<211> 17
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<220>
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<210> 631
<211> 18
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<220>
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<400> 631

gaagggataa tggaatat 18

<210> 632
<211> 17
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<220>
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<400> 632

gaatagtttc gagatga 17

<210> 633
<211> 18
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<220>
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<400> 633

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<210> 634
<211> 16
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<220>
<223> Detection oligonucleotide for ORPHAN NUCLEAR RECEPTOR NR5A2 (ALPHA-1-FETOPROTEIN TRANSCRIPTION FACTOR) (HEPATOCYTIC TRANSCRIPTION FACTOR) (B1-BINDING FACTOR) (HB1F) (CYP7A PROMOTER BINDING FACTOR)

<400> 634

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<210> 635
<211> 18
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<220>
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<400> 635

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<210> 636
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<220>
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<400> 636

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<210> 637
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<400> 637

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<210> 638
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<400> 638

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<210> 639
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<400> 639

ggtgaattta ttgggg 16

<210> 640
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<400> 641

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<210> 642
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<220>
<223> Detection oligonucleotide for PROTEIN-TYROSINE PHOSPHATASE X PRECURSOR (EC 3.1.3.48) (R-PTP-X) (ISLET CELL AUTOANTIGEN RELATED PROTEIN) (ICAAR) (IAR) (PHOGRIN)

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<220>
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PROTEIN) (ICAAR) (IAR) (PHOGRIN)

<400> 643

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<220>
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<220>
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<400> 645

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<210> 646
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<220>
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<400> 646

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<210> 647
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<212> DNA
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<220>
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<400> 647

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<400> 648

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<400> 650

gtcgatttcg ttacgg 16

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<220>
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<400> 651

gttgatttg ttatggg 17

<210> 652
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<220>
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<400> 652

ttcgggtttc gtatta 16

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<220>
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<400> 653

ttttgggttt tgtattag 18

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aattcgcggt ttcgat 16

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<400> 655

aatttgtggt tttgatg 17

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gtcgtttcgc ggagat 16

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gttgttttgt ggagatt 17

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attggtcgat tcgcgg 16

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<400> 659

tattggttga tttgtgg 17

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agcgtttcga tttcgg 16

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agtgttttga ttttggt 17

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atcgagcgtt tcgatt 16

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ggattgagtg ttttgat 17

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attcgcgtat tcgaga 16

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tttgtgtatt tgagagg 17

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<220>
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<400> 666

gacgttcgcg attaaa 16

<210> 667
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<220>
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<400> 667

tggatgtttg tgattaa 17

<210> 668
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<400> 668

aagtcgatat cgcggt 16

<210> 669
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aaaagttgat attgtggt 18

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<400> 670

agcgttcgga agttta 16

<210> 671
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ggagtgtttg gaagtt 16

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tattcggacg gggata 16

<210> 673
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atttggatgg ggatag 16

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gagacgcgta ggttat 16

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gggagatgtg taggtt 16

<210> 676
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tagttttcgg cgaagg 16

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ggtagttttt ggtgaag 17

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aaggcggtga cgtaaa 16

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aaggtggtga tgtaaa 16

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atggcgtaag tacgtt 16

<210> 681
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gatggtgtaa gtatgtt 17

<210> 682
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agtacgttcg ggacga 16

<210> 683
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<220>
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<400> 683

aagtatgttt gggatga 17

<210> 684
<211> 16
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<220>
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<400> 684

atggtattcg ggtcgt 16

<210> 685
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<220>
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<400> 685

tatggtattt gggttgt 17

<210> 686
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<400> 686

ttggagcgtt aagtaa 16

<210> 687
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RECEPTOR DOCKING PROTEIN)

<400> 687

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<400> 688

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<400> 689

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<220>
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<400> 690

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<210> 691
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<220>
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<400> 691

tgtataatga gaggtga 17

<210> 692
<211> 16
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<220>
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<400> 692

atgtttcggg tatgga 16

<210> 693
<211> 16
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<220>
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<400> 693

atgttttggg tatgga 16

<210> 694
<211> 16
<212> DNA
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<220>
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<400> 694

ttttcgagga attcgt 16

<210> 695
<211> 18
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<220>
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<400> 695

tttttgagg aatttgtt 18

<210> 696
<211> 16
<212> DNA
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<220>
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<400> 696

atagttttcg gcgggt 16

<210> 697
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<220>
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<400> 697

tatagttttt ggtgggt 17

<210> 698
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<220>
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<400> 698

tttttcggcg tagata 16

<210> 699
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<210> 700
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<400> 700

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<210> 701
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<400> 701

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<210> 702
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<400> 702

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<210> 703
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<220>
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<400> 703

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<210> 704
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<400> 704

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<210> 705
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<400> 705

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<210> 706
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<400> 706

taggagacgt tacgtt 16

<210> 707
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<400> 707

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<210> 708
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<220>
<223> Detection oligonucleotide for LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32)

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aagaacggac gtgttt 16

<210> 709
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<212> DNA
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<223> Detection oligonucleotide for LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32)

<400> 709

aggaagaatg gatgtg 16

<210> 710
<211> 16
<212> DNA
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<220>
<223> Detection oligonucleotide for LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32)

<400> 710

tttttgcgat agtcgg 16

<210> 711
<211> 17
<212> DNA
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<220>
<223> Detection oligonucleotide for LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32)

<400> 711

gttttgtga tagttgg 17

<210> 712
<211> 16
<212> DNA
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<220>
<223> Detection oligonucleotide for LOW AFFINITY IMMUNOGLOBULIN GAMMA FC REGION RECEPTOR II-A PRECURSOR (FC-GAMMA RII-A) (FCRII-A) (IGG FC RECEPTOR II-A) (FC-GAMMA-RIIA) (CD32) (CDW32)

<400> 712

tagcggcgat ttaagg 16

<210> 713
<211> 17
<212> DNA
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<220>
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<400> 713

gtagtggtga tttaagg 17

<210> 714
<211> 16
<212> DNA
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<220>
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<400> 714

tttacgagcg agtcgt 16

<210> 715
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<212> DNA
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<220>
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<400> 715

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<210> 716
<211> 17
<212> DNA
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<220>
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<400> 716

tttcgatagt atacggg 17

<210> 717
<211> 18
<212> DNA
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<220>
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<400> 717

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<210> 718
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<220>
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<400> 718

aagggagcgt tcgtta 16

<210> 719
<211> 16
<212> DNA
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<220>
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<400> 719

aagggagtgt ttgtta 16

<210> 720
<211> 16
<212> DNA
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<220>
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<400> 720

aataatagcg acgggg 16

<210> 721
<211> 16
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<213> Artificial Sequence

<220>
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<400> 721

taatagtgat gggggt 16

<210> 722
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for HOMEOBOX PROTEIN GSH-2

<400> 722

tttagaatcg tcgagt 16

<210> 723
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for HOMEOBOX PROTEIN GSH-2

<400> 723

agaattgttg agtgaag 17

<210> 724
<211> 17
<212> DNA
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<220>
<223> Detection oligonucleotide for HOMEOBOX PROTEIN GSH-2

<400> 724

tttttcgtcg gttcgta 17

<210> 725
<211> 17
<212> DNA
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<220>
<223> Detection oligonucleotide for HOMEOBOX PROTEIN GSH-2

<400> 725

tttgttggtt tgtagga 17

<210> 726
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
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<400> 726

aggacggcgt ttatta 16

<210> 727
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
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<400> 727

gatgaggatg gtgttt 16

<210> 728
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<220>
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<400> 728

ttcgatttcg gaggat 16

<210> 729
<211> 17
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<220>
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<400> 729

tttgattttg gaggatt 17

<210> 730
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<220>
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<400> 730

ttcgttatcg agagtt 16

<210> 731
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<220>
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<400> 731

gggttttgtt attgaga 17

<210> 732
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<220>
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<400> 732

gacgtgagcg tttagg 16

<210> 733
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<220>
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<400> 733

gatgtgagtg tttaggg 17

<210> 734
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<220>
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<400> 734

tacggagttg gcgtta 16

<210> 735
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<220>
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<400> 735

tttatggagt tggtgt 16

<210> 736
<211> 16
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<220>
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<400> 736

ttggttcgtc gaggat 16

<210> 737
<211> 16
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<220>
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<400> 737

ttggtttgtt gaggat 16

<210> 738
<211> 16
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<220>
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<400> 738

atcgaaatcg tagagg 16

<210> 739
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
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<400> 739

attgaaattg tagaggg 17

<210> 740
<211> 16
<212> DNA
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<220>
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<400> 740

tatggcggtg atcgtt 16

<210> 741
<211> 17
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<220>
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<400> 741

tttatggtgg tgattgt 17

<210> 742
<211> 16
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<220>
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<400> 742

ttacggcgtt tcggat 16

<210> 743
<211> 17
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<220>
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<400> 743

ttatggtgtt ttggatt 17

<210> 744
<211> 16
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<220>
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<400> 744

atgcgtttta cgtcgt 16

<210> 745
<211> 18
<212> DNA
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<220>

<223> Detection oligonucleotide for HISTONE H4

<400> 745

agatgtgttt tatgttgt 18

<210> 746
<211> 16
<212> DNA
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<220>
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<400> 746

taaggcgtcg gatggt 16

<210> 747
<211> 16
<212> DNA
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<220>
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<400> 747

gagtaaggtg ttggat 16

<210> 748
<211> 16
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<220>
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<400> 748

tattttacgg tggcgt 16

<210> 749
<211> 17
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<220>
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<400> 749

attttatggt ggtgttt 17

<210> 750
<211> 16
<212> DNA

<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2)

<400> 750

atttcggagg tatcgt 16

<210> 751
<211> 16
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<220>
<223> Detection oligonucleotide for POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2)

<400> 751

tttggaggta ttgtgt 16

<210> 752
<211> 16
<212> DNA
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<220>
<223> Detection oligonucleotide for POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2)

<400> 752

ttcgtacggg gtatag 16

<210> 753
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
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<400> 753

ggtttgtatg gggtata 17

<210> 754
<211> 16
<212> DNA
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<220>
<223> Detection oligonucleotide for POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2)

<400> 754

tataaggcgt tacggt 16

<210> 755
<211> 17
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<220>
<223> Detection oligonucleotide for POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2)

<400> 755

ggtataaggt gttatgg 17

<210> 756
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<220>
<223> Detection oligonucleotide for POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2)

<400> 756

ttacggtcgc gtagta 16

<210> 757
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for POTASSIUM VOLTAGE-GATED CHANNEL SUBFAMILY KQT MEMBER 2 (NEUROBLASTOMA- SPECIFIC POTASSIUM CHANNEL KQT-LIKE 2)

<400> 757

tatggttgtg tagtagt 17

<210> 758
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA

1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22)

<400> 758

ttattcgtag ttttcgg 17

<210> 759
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22)

<400> 759

gtttatttgt agtttttgg 19

<210> 760
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22)

<400> 760

tgtaatcgtt tattcgt 17

<210> 761
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22)

<400> 761

taattgttta tttgtagttt 20

<210> 762

<211> 16
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<213> Artificial Sequence

<220>
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<400> 762

ttcgaagtcg ggatta 16

<210> 763
<211> 17
<212> DNA
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<220>
<223> Detection oligonucleotide for ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22)

<400> 763

attttgaagt tgggatt 17

<210> 764
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for ADAPTER-RELATED PROTEIN COMPLEX 1 SIGMA 1B SUBUNIT (SIGMA-ADAPTIN 1B) (ADAPTOR PROTEIN COMPLEX AP-1 SIGMA-1B SUBUNIT) (GOLGI ADAPTOR HA1/AP1 ADAPTIN SIGMA-1B SUBUNIT) (CLATHRIN ASSEMBLY PROTEIN COMPLEX 1 SIGMA- 1B SMALL CHAIN) (SIGMA 1B SUBUNIT OF AP-1 CLATHRIN) (DC22)

<400> 764

atcgagagta tttcgaag 18

<210> 765
<211> 18
<212> DNA
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<220>
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<400> 765

ggattgagag tattttga 18

<210> 766
<211> 17
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<220>
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<400> 766

taagcggtat aagtcgg 17

<210> 767
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<220>
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<400> 767

agtggtataa gttggtt 17

<210> 768
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
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<400> 768

ttcggtaagc ggtata 16

<210> 769
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<220>
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<400> 769

ataatttggt aagtggta 18

<210> 770
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<220>
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<400> 770

ttcgtgattt tacgtta 17

<210> 771
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<400> 771

aattttgtga ttttatgtt 19

<210> 772
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<220>
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<400> 772

tggcgacgaa gtgtaa 16

<210> 773
<211> 16
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<220>
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<400> 773

tttgtggtga tgaagt 16

<210> 774
<211> 16
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<220>
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<400> 774

tagcgggttt acggag 16

<210> 775
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agtagtgggt ttatgg 16

<210> 776
<211> 16
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<220>
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<400> 776

taacgagtcg agcgga 16

<210> 777
<211> 16
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<213> Artificial Sequence

<220>
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<400> 777

aatgagttga gtggag 16

<210> 778
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<220>
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<400> 778

ttttcgcgtg taagtt 16

<210> 779
<211> 18
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<220>
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<400> 779

tttttgtgtg taagttaa 18

<210> 780
<211> 16
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<220>
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<400> 780

taggacgatt cggata 16

<210> 781

<211> 17
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<220>
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<400> 781

aggatgattt ggatagt 17

<210> 782
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
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<400> 782

ttcgagtgaa agcggta 17

<210> 783
<211> 17
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<220>
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<400> 783

tttgagtgaa agtggta 17

<210> 784
<211> 17
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)

<400> 784

ttacgttttc gtgaaat 17

<210> 785
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)

<400> 785

ttttatgttt ttgtgaaat 19

<210> 786
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)

<400> 786

gggaggacgt agagta 16

<210> 787
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)

<400> 787

gggaggatgt agagta 16

<210> 788
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)

<400> 788

tgggttatcg tttatatt 18

<210> 789
<211> 19
<212> DNA
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<220>
<223> Detection oligonucleotide for PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)

<400> 789

ttgggttatt gtttatatt 19

<210> 790
<211> 17
<212> DNA
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<220>
<223> Detection oligonucleotide for PERIPLAKIN (195 KDA CORNIFIED ENVELOPE PRECURSOR) (190 KDA PARANEOPLASTIC PEMPHIGUS ANTIGEN)

<400> 790

tggtatcggt ttttgaa 17

<210> 791
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<400> 791

tggtattggt ttttgaa 17

<210> 792
<211> 17
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<400> 792

gtttaggttc gagttta 17

<210> 793
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<400> 793

ggtttaggtt tgagttta 18

<210> 794
<211> 16
<212> DNA
<213> Artificial Sequence

<220>
<223> Detection oligonucleotide for

<400> 794

agaattgcga cggttt 16

<210> 795
<211> 17
<212> DNA
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